FILE 'HOME' ENTERED AT 17:18:33 ON 13 SEP 2008

=> file reg
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'REGISTRY' ENTERED AT 17:18:50 ON 13 SEP 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 12 SEP 2008 HIGHEST RN 1049105-01-2
DICTIONARY FILE UPDATES: 12 SEP 2008 HIGHEST RN 1049105-01-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

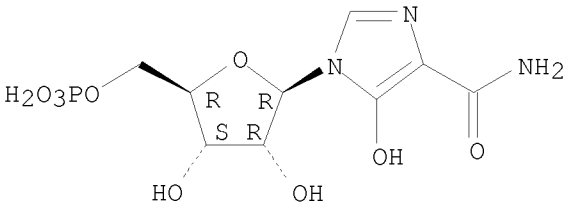
=> s mizoribine
L1 2 MIZORIBINE

=> s indanocine
L2 1 INDANOCINE

=> d l1 1-2

L1 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2008 ACS on STN
RN 62025-48-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-(5-O-phosphono-β-D-
ribofuranosyl)- (CA INDEX NAME)
OTHER NAMES:
CN Bredinin 5'-monophosphate
CN Mizoribine 5'-monophosphate
FS STEREOSEARCH
MF C9 H14 N3 O9 P
CI COM
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, MEDLINE, TOXCENTER,
USPATFULL

Absolute stereochemistry.

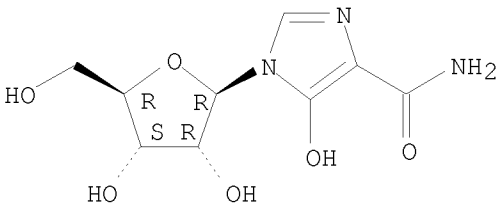


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

20 REFERENCES IN FILE CA (1907 TO DATE)
20 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2008 ACS on STN
RN 50924-49-7 REGISTRY
ED Entered STN: 16 Nov 1984
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)
OTHER NAMES:
CN β-Bredinin
CN Bredinin
CN HE 69
CN Mizoribine
CN NSC 289637
FS STEREOSEARCH
DR 55727-07-6
MF C9 H13 N3 O6
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, NAPRALERT, PHAR, PROMT, PROUSDDR, PS, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

475 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
475 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL

	ENTRY	SESSION
FULL ESTIMATED COST	15.22	15.43

FILE 'CAPLUS' ENTERED AT 17:19:45 ON 13 SEP 2008
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FILE COVERS 1907 - 13 Sep 2008 VOL 149 ISS 12
FILE LAST UPDATED: 12 Sep 2008 (20080912/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/legal/infopolicy.html

=> s l1 <> or mizoribine?

SmartSELECT INITIATED
New TRANSFER and ANALYZE Commands Now Available
See HELP TRANSFER and HELP ANALYZE for Details

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.48	15.91

FILE 'REGISTRY' ENTERED AT 17:19:59 ON 13 SEP 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

SET SMARTSELECT ON
SET COMMAND COMPLETED

SEL L1 1-
L3 SEL L1 1- CHEM : 10 TERMS

SET SMARTSELECT OFF
SET COMMAND COMPLETED

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	12.11	28.02

FILE 'CAPLUS' ENTERED AT 17:20:00 ON 13 SEP 2008

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

S L3 OR MIZORIBINE?

437 MIZORIBINE?
L5 564 L4 OR MIZORIBINE?

=> s l2 <> or indanocine?

SmartSELECT INITIATED
New TRANSFER and ANALYZE Commands Now Available
See HELP TRANSFER and HELP ANALYZE for Details

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	38.64	66.66

FILE 'REGISTRY' ENTERED AT 17:20:14 ON 13 SEP 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 American Chemical Society (ACS)

SET SMARTSELECT ON
SET COMMAND COMPLETED

SEL L2 1-
L6 SEL L2 1- CHEM : 3 TERMS

SET SMARTSELECT OFF
SET COMMAND COMPLETED

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	12.11	78.77

FILE 'CAPLUS' ENTERED AT 17:20:15 ON 13 SEP 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

S L6 OR INDANOCINE?

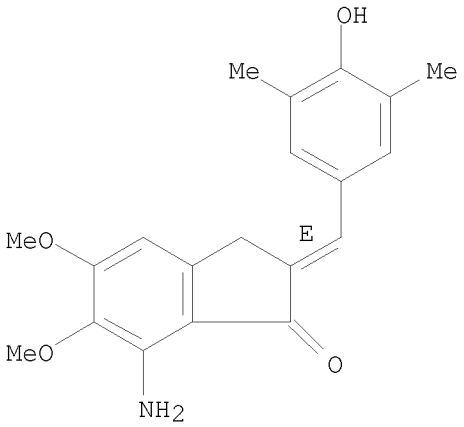
33 INDANOCINE?
L8 38 L7 OR INDANOCINE?

=> d l2
YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:y

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
RN 265646-19-3 REGISTRY
ED Entered STN: 19 May 2000
CN 1H-Inden-1-one, 7-amino-2,3-dihydro-2-[(4-hydroxy-3,5-

dimethylphenyl)methylene]-5,6-dimethoxy-, (2E)- (CA INDEX NAME)
OTHER NAMES:
CN Indanocine
CN NSC 698666
FS STEREOSEARCH
MF C20 H21 N O4
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, TOXCENTER, USPATFULL

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

34 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
36 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.48	92.79

FILE 'CAPLUS' ENTERED AT 17:21:17 ON 13 SEP 2008

FILE COVERS 1907 - 13 Sep 2008 VOL 149 ISS 12
FILE LAST UPDATED: 12 Sep 2008 (20080912/ED)

Caplus now includes complete International Patent Classification (IPC)

reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/legal/infopolicy.html

```
=> d his

     (FILE 'HOME' ENTERED AT 17:18:33 ON 13 SEP 2008)

     FILE 'REGISTRY' ENTERED AT 17:18:50 ON 13 SEP 2008
L1             2 S MIZORIBINE
L2             1 S INDANOCINE

     FILE 'CAPLUS' ENTERED AT 17:19:45 ON 13 SEP 2008

     FILE 'REGISTRY' ENTERED AT 17:19:59 ON 13 SEP 2008
                SET SMARTSELECT ON
L3           SEL L1 1- CHEM :      10 TERMS
                SET SMARTSELECT OFF

     FILE 'CAPLUS' ENTERED AT 17:20:00 ON 13 SEP 2008
L4           564 S L3
L5           564 S L4 OR MIZORIBINE?

     FILE 'REGISTRY' ENTERED AT 17:20:14 ON 13 SEP 2008
                SET SMARTSELECT ON
L6           SEL L2 1- CHEM :       3 TERMS
                SET SMARTSELECT OFF

     FILE 'CAPLUS' ENTERED AT 17:20:15 ON 13 SEP 2008
L7            38 S L6
L8            38 S L7 OR INDANOCINE?

     FILE 'REGISTRY' ENTERED AT 17:21:03 ON 13 SEP 2008

     FILE 'CAPLUS' ENTERED AT 17:21:03 ON 13 SEP 2008

     FILE 'CAPLUS' ENTERED AT 17:21:17 ON 13 SEP 2008

=> s l5 or bredinin or he 69 or nsc 289637
           135 BREDININ
        198720 HE
          2209 HES
        200856 HE
                  (HE OR HES)
        156027 69
             0 HE 69
                  (HE(W)69)
          4300 NSC
           812 NSCS
          4814 NSC
                  (NSC OR NSCS)
             1 289637
             0 NSC 289637
                  (NSC(W)289637)
L9           564 L5 OR BREDININ OR HE 69 OR NSC 289637

=> s l8 or nsc 698666
          4300 NSC
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```
           812 NSCS
          4814 NSC
                 (NSC OR NSCS)
             0 698666
             0 NSC 698666
                 (NSC(W)698666)
L10         38 L8 OR NSC 698666

=> s l9 and (cancer or tumor or neoplasm or neoplastic or tumour or sarcoma or
leukemia or leukemic or neoplastic)
        374278 CANCER
         55038 CANCERS
        388073 CANCER
                 (CANCER OR CANCERS)
        466303 TUMOR
        173294 TUMORS
        519563 TUMOR
                 (TUMOR OR TUMORS)
        511574 NEOPLASM
         37380 NEOPLASMS
        528590 NEOPLASM
                 (NEOPLASM OR NEOPLASMS)
         65985 NEOPLASTIC
            22 NEOPLASTICS
         66001 NEOPLASTIC
                 (NEOPLASTIC OR NEOPLASTICS)
          3901 TUMOUR
          1463 TUMOURS
          5271 TUMOUR
                 (TUMOUR OR TUMOURS)
         42771 SARCOMA
          4636 SARCOMAS
           106 SARCOMATA
         44496 SARCOMA
                 (SARCOMA OR SARCOMAS OR SARCOMATA)
        115845 LEUKEMIA
          7723 LEUKEMIAS
        117342 LEUKEMIA
                 (LEUKEMIA OR LEUKEMIAS)
         19978 LEUKEMIC
            26 LEUKEMICS
         19991 LEUKEMIC
                 (LEUKEMIC OR LEUKEMICS)
         65985 NEOPLASTIC
            22 NEOPLASTICS
         66001 NEOPLASTIC
                 (NEOPLASTIC OR NEOPLASTICS)
L11         95 L9 AND (CANCER OR TUMOR OR NEOPLASM OR NEOPLASTIC OR TUMOUR OR
               SARCOMA OR LEUKEMIA OR LEUKEMIC OR NEOPLASTIC)

=> s l10 and (cancer or tumor or neoplasm or neoplastic or tumour or sarcoma or
leukemia or leukemic or neoplastic)
        374278 CANCER
         55038 CANCERS
        388073 CANCER
                 (CANCER OR CANCERS)
        466303 TUMOR
        173294 TUMORS
        519563 TUMOR
                 (TUMOR OR TUMORS)
        511574 NEOPLASM
```

```
         37380 NEOPLASMS
        528590 NEOPLASM
                 (NEOPLASM OR NEOPLASMS)
         65985 NEOPLASTIC
            22 NEOPLASTICS
         66001 NEOPLASTIC
                 (NEOPLASTIC OR NEOPLASTICS)
          3901 TUMOUR
          1463 TUMOURS
          5271 TUMOUR
                 (TUMOUR OR TUMOURS)
         42771 SARCOMA
          4636 SARCOMAS
           106 SARCOMATA
         44496 SARCOMA
                 (SARCOMA OR SARCOMAS OR SARCOMATA)
        115845 LEUKEMIA
          7723 LEUKEMIAS
        117342 LEUKEMIA
                 (LEUKEMIA OR LEUKEMIAS)
         19978 LEUKEMIC
            26 LEUKEMICS
         19991 LEUKEMIC
                 (LEUKEMIC OR LEUKEMICS)
         65985 NEOPLASTIC
            22 NEOPLASTICS
         66001 NEOPLASTIC
                 (NEOPLASTIC OR NEOPLASTICS)
L12         14 L10 AND (CANCER OR TUMOR OR NEOPLASM OR NEOPLASTIC OR TUMOUR OR
               SARCOMA OR LEUKEMIA OR LEUKEMIC OR NEOPLASTIC)

=> d his

     (FILE 'HOME' ENTERED AT 17:18:33 ON 13 SEP 2008)

     FILE 'REGISTRY' ENTERED AT 17:18:50 ON 13 SEP 2008
L1             2 S MIZORIBINE
L2             1 S INDANOCINE

     FILE 'CAPLUS' ENTERED AT 17:19:45 ON 13 SEP 2008

     FILE 'REGISTRY' ENTERED AT 17:19:59 ON 13 SEP 2008
                 SET SMARTSELECT ON
L3           SEL L1 1- CHEM :      10 TERMS
                 SET SMARTSELECT OFF

     FILE 'CAPLUS' ENTERED AT 17:20:00 ON 13 SEP 2008
L4           564 S L3
L5           564 S L4 OR MIZORIBINE?

     FILE 'REGISTRY' ENTERED AT 17:20:14 ON 13 SEP 2008
                 SET SMARTSELECT ON
L6           SEL L2 1- CHEM :       3 TERMS
                 SET SMARTSELECT OFF

     FILE 'CAPLUS' ENTERED AT 17:20:15 ON 13 SEP 2008
L7            38 S L6
L8            38 S L7 OR INDANOCINE?

     FILE 'REGISTRY' ENTERED AT 17:21:03 ON 13 SEP 2008
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     FILE 'CAPLUS' ENTERED AT 17:21:03 ON 13 SEP 2008

     FILE 'CAPLUS' ENTERED AT 17:21:17 ON 13 SEP 2008
L9          564 S L5 OR BREDININ OR HE 69 OR NSC 289637
L10          38 S L8 OR NSC 698666
                E TUMOR+ALL/CT
                E CANCER+ALL/CT
                E NEOPLASM+ALL/CT
                E LEUKEMIA+ALL/CT
L11          95 S L9 AND (CANCER OR TUMOR OR NEOPLASM OR NEOPLASTIC OR TUMOUR O
L12          14 S L10 AND (CANCER OR TUMOR OR NEOPLASM OR NEOPLASTIC OR TUMOUR

=> s l11 and l12
L13           2 L11 AND L12

=> d ibib abs

L13  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2004:120750  CAPLUS
DOCUMENT NUMBER:          140:175121
TITLE:                    Therapeutic inhibition of protein kinases and a
                          cellular ATP synthetic pathway in cancer
                          cells
INVENTOR(S):              Carson, Dennis A.; Rosenbach, Michael D.; Carrera,
                          Carlos J.; Leoni, Lorenzo M.
PATENT ASSIGNEE(S):       The Regents of the University of California, USA;
                          Salmedix, Inc.
SOURCE:                   PCT Int. Appl., 66 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2004012769         A1    20040212    WO 2003-US24439         20030801
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2003258061         A1    20040223    AU 2003-258061          20030801
     US 20040096436        A1    20040520    US 2003-632592          20030801
PRIORITY APPLN. INFO.:                       US 2002-400568P     P   20020802
                                             WO 2003-US24439     W   20030801
AB   The present invention provides methods of treating cancer using
     inhibitors of protein kinases.  The inhibitors of protein kinases are
     combined with agents that inhibit a cellular ATP synthetic pathway.
     Inhibitors of ATP synthesis include inhibitors of de novo purine
     biosynthesis, inhibitors of the salvage pathway of ATP biosynthesis, and
     inhibitors of the enzyme inosine monophosphate dehydrogenase.


=> d ibib abs 2
```

L13 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:120731 CAPLUS
DOCUMENT NUMBER: 140:157496
TITLE: Inosine monophosphate dehydrogenase inhibitors and prodrugs in the treatment of cancer and immune disease
INVENTOR(S): Carson, Dennis A.; Leoni, Lorenzo M.; Cottam, Howard B.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004012746	A2	20040212	WO 2003-US24325		20030801
WO 2004012746	A3	20040805			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003261354	A1	20040223	AU 2003-261354		20030801
US 20040127435	A1	20040701	US 2003-632711		20030801
PRIORITY APPLN. INFO.:			US 2002-400583P	P	20020802
			WO 2003-US24325	W	20030801

OTHER SOURCE(S): MARPAT 140:157496
AB The invention provides methods of treating cancer using inhibitors of inosine monophosphate dehydrogenase (IMPDH). The IMPDH inhibitors are combined with compds. that inhibit cellular processes regulated by GTP or ATP. Also provided are prodrugs of the IMPDH inhibitor mizoribine and its aglycon. The prodrugs are useful in practicing the methods of the invention, including immunosuppressive therapy and treatment of cancer by prolonged administration without addnl. therapeutic compds.

=> d his

(FILE 'HOME' ENTERED AT 17:18:33 ON 13 SEP 2008)

FILE 'REGISTRY' ENTERED AT 17:18:50 ON 13 SEP 2008
L1 2 S MIZORIBINE
L2 1 S INDANOCINE

FILE 'CAPLUS' ENTERED AT 17:19:45 ON 13 SEP 2008

FILE 'REGISTRY' ENTERED AT 17:19:59 ON 13 SEP 2008
SET SMARTSELECT ON
L3 SEL L1 1- CHEM : 10 TERMS
SET SMARTSELECT OFF

FILE 'CAPLUS' ENTERED AT 17:20:00 ON 13 SEP 2008

```
L4          564 S L3
L5          564 S L4 OR MIZORIBINE?

     FILE 'REGISTRY' ENTERED AT 17:20:14 ON 13 SEP 2008
                SET SMARTSELECT ON
L6          SEL L2 1- CHEM :       3 TERMS
                SET SMARTSELECT OFF

     FILE 'CAPLUS' ENTERED AT 17:20:15 ON 13 SEP 2008
L7           38 S L6
L8           38 S L7 OR INDANOCINE?

     FILE 'REGISTRY' ENTERED AT 17:21:03 ON 13 SEP 2008

     FILE 'CAPLUS' ENTERED AT 17:21:03 ON 13 SEP 2008

     FILE 'CAPLUS' ENTERED AT 17:21:17 ON 13 SEP 2008
L9          564 S L5 OR BREDININ OR HE 69 OR NSC 289637
L10          38 S L8 OR NSC 698666
                E TUMOR+ALL/CT
                E CANCER+ALL/CT
                E NEOPLASM+ALL/CT
                E LEUKEMIA+ALL/CT
L11          95 S L9 AND (CANCER OR TUMOR OR NEOPLASM OR NEOPLASTIC OR TUMOUR O
L12          14 S L10 AND (CANCER OR TUMOR OR NEOPLASM OR NEOPLASTIC OR TUMOUR
L13           2 S L11 AND L12

=> s l11 and pd<=2002
      22911506 PD<=2002
                  (PD<=20029999)
L14         58 L11 AND PD<=2002

=> s l12 and pd<=2002
      22911506 PD<=2002
                  (PD<=20029999)
L15          3 L12 AND PD<=2002

=> focus l14
PROCESSING COMPLETED FOR L14
L16          58 FOCUS L14 1-

=> d ibib abs hitstr 1-58

L16  ANSWER 1 OF 58  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        2004:119752  CAPLUS
DOCUMENT NUMBER:         140:162347
TITLE:                   Compositions comprising tumor-dendritic
                         Fusion cells, recombinant human interleukin 12,
                         antipyretic and immunosuppressant for cancer
                         immunotherapy
INVENTOR(S):             Ohno, Tsuneya
PATENT ASSIGNEE(S):      USA
SOURCE:                  U.S. Pat. Appl. Publ., 38 pp., Cont.-in-part of U.S.
                         Ser. No. 12,134.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  2
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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US 20040028663	A1	20040212	US 2002-328998		20021224
US 20020168351	A1	20021114	US 2001-12134		20011022 <--
PRIORITY APPLN. INFO.:			US 2000-242154P	P	20001020
			US 2001-12134	A2	20011022

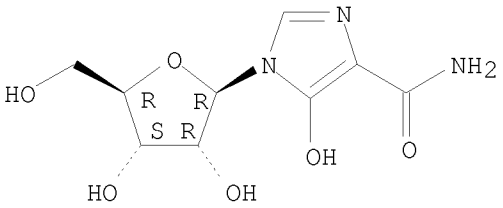
AB The present invention relates to methods and compns. for treating and preventing cancer by administering a therapeutically ED of fusion cells formed by fusion of autologous dendritic cells and autologous non-dendritic cells, in combination with a cytokine or other mol. which stimulates or induces a cytotoxic T cell response and/or a humoral immune response.

IT 50924-49-7, Mizoribine
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising tumor-dendritic Fusion cells, recombinant human interleukin 12, antipyretic and immunosuppressant for cancer immunotherapy)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 2 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

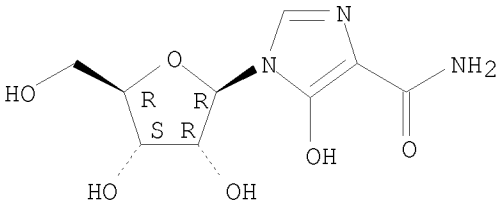
ACCESSION NUMBER:	1984:61457 CAPLUS
DOCUMENT NUMBER:	100:61457
ORIGINAL REFERENCE NO.:	100:9249a,9252a
TITLE:	Genetic and biochemical studies on the activation and cytotoxic mechanism of bredinin, a potent inhibitor of purine biosynthesis in mammalian cells
AUTHOR(S):	Koyama, Hideki; Tsuji, Masae
CORPORATE SOURCE:	Cancer Inst., Japanese Found. Cancer Res., Tokyo, 170, Japan
SOURCE:	Biochemical Pharmacology (1983), 32(23), 3547-53 CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB To study the activation and cytotoxic mechanism of bredinin [50924-49-7], a novel nucleoside antibiotic with potent cytotoxic and immunosuppressive effects, 5 mutants resistant to 10 μM bredinin were isolated from cultured mouse mammary carcinoma FM3A cells mutagenized with N-methyl-N'-nitro-N-nitrosoguanidine. Such bredinin-resistant (Brdr) mutants were 15- to 19-fold less sensitive to the antibiotic than wild-type cells and maintained stably their resistant phenotypes in the absence of bredinin for more than 3 mo. They were cross-resistant to tubercidin [69-33-0], an adenosine analog. Like wild-type cells, Brdr mutants were capable of incorporating radioactivity from ring-labeled adenosine [58-61-7] into the acid-insol. macromol. fraction. However, hypoxanthine-guanine phosphoribosyltransferase [9016-12-0]-deficient mutants derived from the

Brdr cells did not incorporate the radioactivity at all or at a markedly reduced rate, indicating that blockade of the pathway via adenosine deaminase [9026-93-1] present in the Brdr cells resulted in loss of their ability to utilize adenosine. Enzyme assays using cell-free exts. revealed that all the Brdr mutants had <3% of the adenosine kinase (AK) [9027-72-9] activity found in wild-type cells. These results demonstrate that the bredinin resistance is attributed to a defective AK activity and, therefore, that bredinin is metabolized by AK, which may phosphorylate it to a toxic nucleotide, bredinin 5'-monophosphate (Brd-MP) [62025-48-3], in sensitive cells. Among exogenously added purine bases, guanine [73-40-5] was able to reverse the cytotoxic effect of bredinin on both wild-type cells and F5 cells carrying the vector pSV2-Escherichia coli xanthine-guanine phosphoribosyltransferase [9023-10-3] gene, while xanthine [69-89-6] was able to do so only in F5 cells because the base was metabolized to XMP [523-98-8] by the cells. Apparently, the cytotoxicity of bredinin is due to the formation of Brd-MP in sensitive cells which blocks the conversion of IMP [131-99-7] to XMP by inhibiting IMP dehydrogenase [9028-93-7].

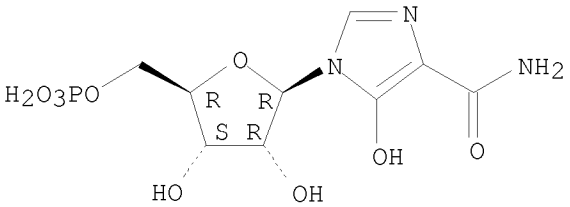
IT 50924-49-7
RL: PRP (Properties)
(cytotoxicity of, purine formation and genetics in relation to)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



IT 62025-48-3
RL: FORM (Formation, nonpreparative)
(formation of, as bredinin metabolite, resistance in relation to)
RN 62025-48-3 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-(5-O-phosphono-β-D-ribofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.



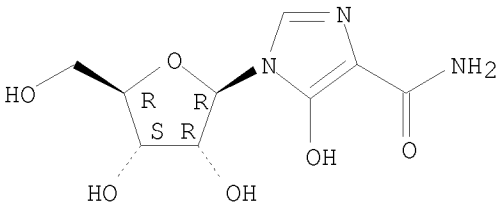
L16 ANSWER 3 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:207255 CAPLUS
DOCUMENT NUMBER: 116:207255
ORIGINAL REFERENCE NO.: 116:34871a,34874a

TITLE: A sequential immunosuppressive treatment with Mizoribine (Bredinin) plus Cyclosporin A on the subrenal capsule assay
AUTHOR(S): Ushijima, Kimio; Nishida, Takashi; Oda, Takaaki; Sugiyama, Toru; Yakushiji, Michiaki
CORPORATE SOURCE: Dep. Obstet. Gynecol., Natl. Kokura Hosp., Kitakyushu, 802, Japan
SOURCE: Kurume Medical Journal (1991), 38(3), 195-8
CODEN: KRMJAC; ISSN: 0023-5679
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To minimize immunol. interferences on the subrenal capsule (SRC) assay, a new immunosuppressor, Mizoribine (MZB: Bredinin) alone or combined with cyclosporin A (ScA) was evaluated by an exptl. SRC assay system using a rat ovarian cancer tissue. Daily applications of MZB (200 mg/kg) for 7 days following the xenograft of cancer tissue were insufficient to suppress immunol. reactions of the recipient mice, and all the grafted cancer tissues were rejected. Although CsA monotreatment (60 mg/kg of CsA given daily for 7 days) successfully suppressed the host immune reaction, enhanced toxicities of CsA in combination with anticancer agents caused high lethal rate of host mice during the exptl. chemotherapy. Sequential use of CsA on day 0 to day 2 followed by MZB on day 3, 5 and 7 brought the most favorable results with minimal host reactions and toxicities. An anticancer screening test using the modified SRCA accurately reflected the results of exptl. chemotherapy against the rat ovarian cancer. The results suggest that the sequential treatment of MZB and CsA is a feasible immunosuppressive treatment which minimizes immunol. interferences with SRC assay chemoscreening test.

IT 50924-49-7
RL: ANST (Analytical study)
(immunosuppression from cyclosporin A and, in neoplasm inhibitor evaluation in subrenal capsule assay)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



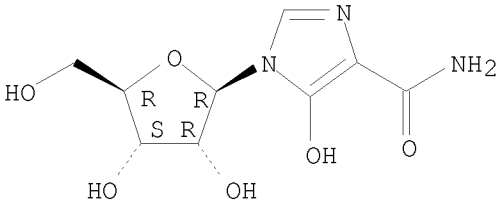
L16 ANSWER 4 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:778110 CAPLUS
DOCUMENT NUMBER: 128:97431
ORIGINAL REFERENCE NO.: 128:18905a
TITLE: Differentiation induction in non-lymphocytic leukemia cells upon treatment with mizoribine
AUTHOR(S): Inai, Kunihiro; Tsutani, Hiroshi; Yamauchi, Takahiro; Huberman, Eliezer; Nakamura, Toru; Ueda, Takanori
CORPORATE SOURCE: First Department of Internal Medicine, Fukui Medical School, Fukui, 910-11, Japan
SOURCE: International Journal of Hematology (1997),

66(3), 335-344
CODEN: IJHEEY; ISSN: 0925-5710
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Inosine-5'-monophosphate (IMP) dehydrogenase catalyzes the rate-limiting reaction of guanine nucleotide biosynthesis and has been implicated in the reaction of cell growth and differentiation. We examined the ability of mizoribine, an IMP dehydrogenase inhibitor, to induce differentiation in HL-60 and U937 cells as well as in fresh leukemic blast cells from patients with non-lymphocytic leukemia. Treatment with mizoribine reduced intracellular GTP levels and induced morphol. and functional differentiation in these two cell lines in a dose-dependent manner. HL-60 and U937 cells developed polymorphic nuclei and macrophage-like cytoplasm, resp., as well as expression of CD11b and CD14 antigens and the ability to oxidize NBT. These changes became evident when intracellular GTP levels decreased to approx. 30% of untreated controls and were abrogated by addition of guanosine to the media. However, in fresh leukemic cells, the cells showing maturation in response to mizoribine were limited in those derived from two of ten patients having non-lymphocytic leukemia. These findings suggest mizoribine could induce differentiation in HL-60 and U937 cells through a decrease of intracellular GTP levels. Further study is required to determine its clin. use in patients with acute non-lymphocytic leukemia.

IT 50924-49-7, Mizoribine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(mizoribine induces differentiation of human, non-lymphocytic leukemia cells)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

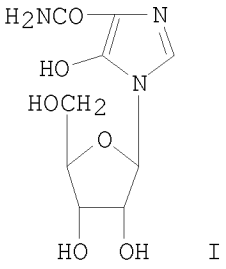
Absolute stereochemistry.



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1977:83546 CAPLUS
DOCUMENT NUMBER: 86:83546
ORIGINAL REFERENCE NO.: 86:13137a,13140a
TITLE: Mode of action of bredinin with guanylic acid on L5178Y mouse leukemia cells
AUTHOR(S): Sakaguchi, Kengo; Tsujino, Masatoshi; Hayashi, Mitsuo; Kawai, Kunio; Mizuno, Kimio; Hayano, Kazuo
CORPORATE SOURCE: Res. Lab., Toyo Jozo Co., Ltd., Ohito, Japan
SOURCE: Journal of Antibiotics (1976), 29(12), 1320-7
CODEN: JANTAJ; ISSN: 0021-8820
DOCUMENT TYPE: Journal

LANGUAGE: English
GI



I

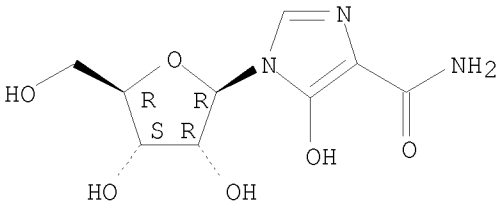
AB Bredinin (I) [50924-49-7] (1.2 + 10-5M) inhibited nucleic acid formation and the growth of leukemic cells by causing chromosomal aberrations. These effects of I were counteracted by GMP [85-32-5]. I was cytotoxic at >2 + 10-5M but was cytostatic at 5 + 10-5M in the presence of GMP. The cytostatic effect of I in the presence of GMP was completely reversed by cyclic AMP [60-92-4]. The effect of cyclic AMP depended upon the concentration of GMP present; the effect was not observed in the absence of GMP.

IT 50924-49-7
RL: BIOL (Biological study)
(leukemia inhibition by, GMP effect on)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 6 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:508593 CAPLUS
DOCUMENT NUMBER: 111:108593
ORIGINAL REFERENCE NO.: 111:18039a,18042a
TITLE: Dual inhibitory effect of bredinin
AUTHOR(S): Kusumi, T.; Tsuda, M.; Katsunuma, T.; Yamamura, M.
CORPORATE SOURCE: Sch. Med., Tokai Univ., Kanagawa, 259-11, Japan
SOURCE: Cell Biochemistry and Function (1989), 7(3), 201-4
CODEN: CBFUDH; ISSN: 0263-6484
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bredinin inhibition of cell growth was investigated in the mouse lymphoma cell line L5178Y. Bredinin caused the accumulation of IMP and the reduction of XMP. It was converted to the 5'-phosphate within the cells. Bredinin 5'-phosphate but not bredinin competitively inhibited both IMP dehydrogenase and GMP synthetase. Thus, the inhibition of cell growth is probably due to bredinin

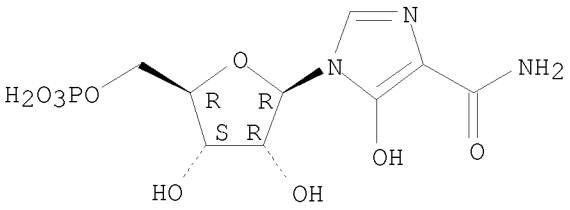
5'-phosphate, which inhibits the consecutive enzyme reactions IMP dehydrogenase and GMP synthetase. These inhibitions result in the accumulation of IMP and the reduction of XMP.

IT 62025-48-3
RL: BIOL (Biological study)
(GMP synthetase and IMP dehydrogenase inhibition by, as bredinin metabolite)

RN 62025-48-3 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-(5-O-phosphono-β-D-ribofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.

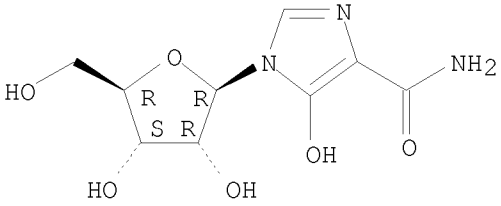


IT 50924-49-7, Bredinin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm inhibition by, purine nucleotide metabolism in)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 7 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1985:137841 CAPLUS

DOCUMENT NUMBER: 102:137841

ORIGINAL REFERENCE NO.: 102:21563a,21566a

TITLE: Sustained-release oral formulations containing bredinin

PATENT ASSIGNEE(S): Toyo Jozo Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

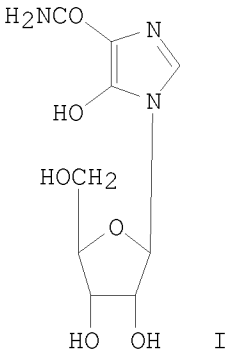
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 59227817	A	19841221	JP 1983-102175	19830607 <--
JP 05030810	B	19930511		

PRIORITY APPLN. INFO.: JP 1983-102175 19830607
GI



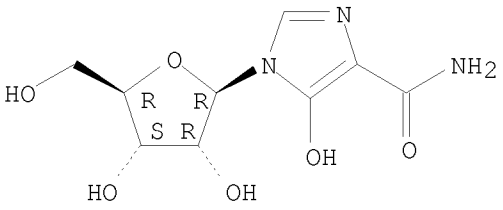
AB Sustained-release enteric formulations contain antitumor bredinin (I) [50924-49-7] coated with polymers semi-permeable to I. Thus, 50 g I and 50 g mannitol were mixed with 5% TC-5R (2-hydroxypropyl Me cellulose [9004-65-3]). The mixture was granulated, dried, pulverized, and added to 1.5% polyisobutylene cyclohexane solution (200 mL) containing 5 g Et cellulose [9004-57-3]. The granules were isolated, dried, and coated with Et cellulose.

IT 50924-49-7
RL: BIOL (Biological study)
(sustained-release pharmaceuticals containing, celluloses and polymer coating of)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 8 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:825220 CAPLUS

DOCUMENT NUMBER: 137:41408

TITLE: Mizoribine, an inhibitor of inosine monophosphate dehydrogenase, inhibits interleukin-6 production by freshly prepared rheumatoid synovial cells

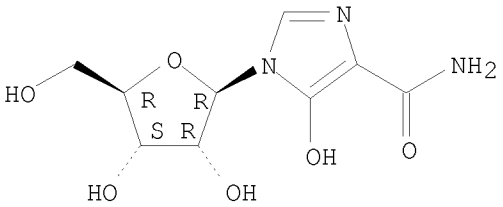
AUTHOR(S): Sugiyama, Eiji; Ikemoto, Masahito; Taki, Hirofumi; Maruyama, Muneharu; Yamashita, Naohiro; Kobayashi, Masashi

CORPORATE SOURCE: First Department of Internal Medicine, Toyama Medical and Pharmaceutical University, Toyama, 930-0194, Japan

SOURCE: Modern Rheumatology (2001), 11(1), 28-33
CODEN: MROHA4; ISSN: 1439-7595

PUBLISHER: Springer-Verlag Tokyo
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mizoribine, an immunosuppressive drug, has been used for treatment in organ transplantation, lupus nephritis, and rheumatoid arthritis (RA). On the basis of in vitro expts., mizoribine has been postulated to be an inhibitor of inosine monophosphate (IMP) dehydrogenase, a pivotal enzyme in the formation of guanine ribonucleotides from IMP. To further characterize the mechanism of the antirheumatic action of this drug, we examined the effect of mizoribine on the production of interleukin (IL)-6, a major inflammatory cytokine in rheumatoid synovia, by freshly prepared rheumatoid synovial cells (RSC). Mizoribine (1.25-5 μg/mL) was able to inhibit the spontaneous production of IL-6 by fresh RSC in a dose-response fashion. The addition of guanosine monophosphate (GMP) reversed its inhibitory effects. In addition, mizoribine inhibited the enhanced production of IL-6 by the IL-1α and/or tumor necrosis factor α-stimulated RSC. Inhibition was also observed at the mRNA level, determined by Northern blot anal. In contrast, mizoribine did not affect IL-8 production by these cells. These data suggest that mizoribine inhibits IL-6 production by fresh RSC, possibly owing to the depletion of intracellular GMP, and that this inhibitory effect of the drug on rheumatoid synovial cells may be related to its efficacy in RA.
IT 50924-49-7, Mizoribine
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mizoribine antirheumatic action mechanism of mizoribine, an inhibitor of IMP dehydrogenase)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



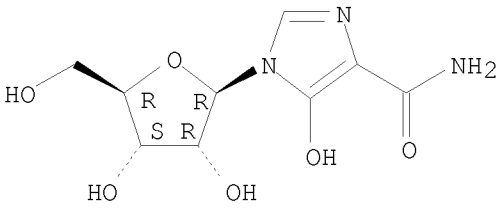
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1980:568561 CAPLUS
DOCUMENT NUMBER: 93:168561
ORIGINAL REFERENCE NO.: 93:26863a,26866a
TITLE: Platinum-bredinin complex
PATENT ASSIGNEE(S): Toyo Jozo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

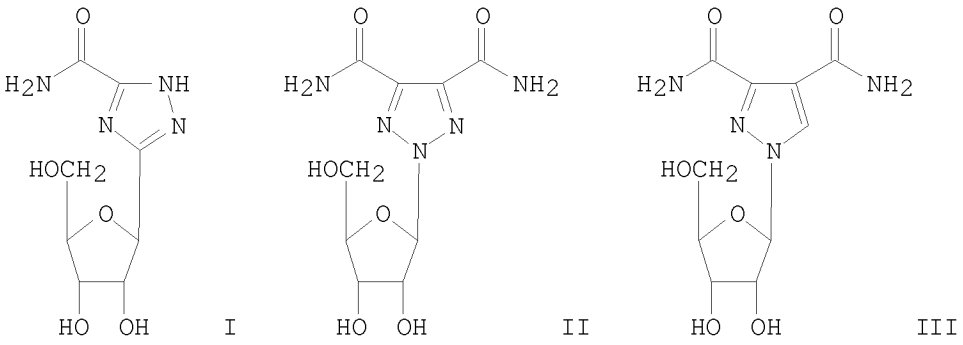
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

JP 55047696 A 19800404 JP 1978-120673 19780929 <--
PRIORITY APPLN. INFO.: JP 1978-120673 A 19780929
AB An aqueous mixture of 100 mg cis-dichlorodiammine platinum(II) and 110 mg AgNO3 was stirred overnight at room temperature, filtered, 0.1 N HCl added to the filtrate, the mixture filtered, 850 mg bredinin added to the resulting diaquodiammine platinum(II) nitrate solution, and the whole stirred 1 wk at room temperature in the dark to give, after chromatog. over SiO2 gel, 150 mg Pt-bredinin complex. An inhibitory ratio of the product was 20 μg Pt/mL against L5178Y cancer cells.
IT 50924-49-7DP, platinum complexes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and anticancer activity of)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 10 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:171869 CAPLUS
DOCUMENT NUMBER: 112:171869
ORIGINAL REFERENCE NO.: 112:28811a,28814a
TITLE: Inhibition of pyrimidine metabolism in myeloid leukemia cells by triazole and pyrazole nucleosides
AUTHOR(S): Matsumoto, Steven S.; Fujitaki, James M.; Nord, L. Dee; Willis, Randall C.; Lee, Vincent M.; Sharma, Brahma S.; Sanghvi, Yogesh S.; Kini, Ganesh D.; Revankar, Ganapathi R.; et al.
CORPORATE SOURCE: Nucleic Acid Res. Inst., Costa Mesa, CA, 92626, USA
SOURCE: Biochemical Pharmacology (1990), 39(3), 455-62
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



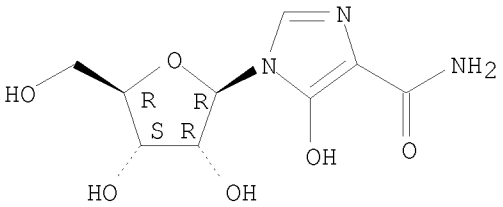
AB Two triazole nucleosides, 3-β-D-ribofuranosyl-1,2,4-triazole-5-carboxamide (I) and 2-β-D-ribofuranosyl-1,2,3-triazole-4,5-dicarboxamide (II) and a pyrazole nucleoside, 1-β-D-ribofuranosylpyrazole-3,4-dicarboxamide (III) inhibited pyrimidine nucleotide biosynthesis in the human myeloid leukemia cell line, K562. Cells treated with these inhibitors released orotate in quantities of 8-35 nmol/105 cells/day. Treatment with these compds. caused the K562 cells to accumulate in the S phase of the cell cycle and induced the cells to synthesize Hb.

IT 50924-49-7, Bredinin
RL: BIOL (Biological study)
(pyrimidine metabolism response to, in human myeloid leukemia cells)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 11 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1980:630776 CAPLUS

DOCUMENT NUMBER: 93:230776

ORIGINAL REFERENCE NO.: 93:36739a,36742a

TITLE: Antitumor activities of newly synthesized 5-carbamoyl-1H-imidazol-4yl 1-adamantanecarboxylate and 5-carbamoyl-1H-imidazol-4yl piperonylate

AUTHOR(S): Yoshida, Noboru; Kiyohara, Takao; Fukui, Masaru; Atsumi, Toshio; Ogino, Shigeo; Inaba, Makoto; Tsukagoshi, Shigeru; Sakurai, Yoshio

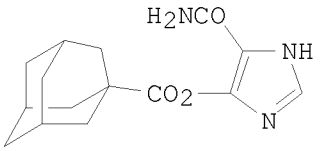
CORPORATE SOURCE: Res. Dep., Sumitomo Chem. Co., Ltd., Takarazuka, 665, Japan

SOURCE: Cancer Research (1980), 40(10), 3810-14
CODEN: CNREA8; ISSN: 0008-5472

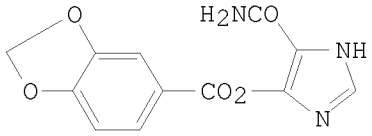
DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I



II

AB The nucleoside antibiotic bredinin, 2 new derivs. SL-1233 (I) [66148-57-0] and SL-1250 (II) [66148-63-8] possessed a potent antitumor activity in several exptl. tumor systems, even though bredinin itself shows only in vitro cytotoxicity and thus lacks therapeutic effectiveness. These 2 derivs. of bredinin exhibited antitumor activity against a wide variety of tumors, including leukemias L-1210 and P388, Lew lung carcinoma, B16 melanoma, Colon 26 and 38 adenocarcinomas, Ehrlich carcinoma, and Sarcoma 180. These agents showed good therapeutic effects not only against ascitic types of tumors but also against a number of slow-growing solid tumor lines, particularly the ascitic and solid forms of Ehrlich carcinoma. At their optimal doses, both compds. effected a complete cure of all or most of the mice treated. They suppressed in vivo tumor growth, presumably by being slowly anabolized in vivo to an active form and inhibiting purine de novo synthesis as bredinin does.

L16 ANSWER 12 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:149471 CAPLUS
DOCUMENT NUMBER: 106:149471
ORIGINAL REFERENCE NO.: 106:24225a,24228a
TITLE: Antitumor, antimetastatic, and antiviral nucleoside-phospholipid complexes
PATENT ASSIGNEE(S): Toyo Jozo Co., Ltd., Japan
SOURCE: Ger. Offen., 26 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3612636	A1	19861106	DE 1986-3612636	19860415 <--
DE 3612636	C2	19931118		
JP 61236793	A	19861022	JP 1985-78283	19850415 <--
JP 05060476	B	19930902		
JP 62099393	A	19870508	JP 1985-237695	19851025 <--
FR 2580283	A1	19861017	FR 1986-5371	19860415 <--
FR 2580283	B1	19891124		
GB 2175588	A	19861203	GB 1986-9112	19860415 <--
GB 2175588	B	19880810		
US 4797479	A	19890110	US 1986-852881	19860415 <--
JP 04210993	A	19920803	JP 1991-39429	19910208 <--

PRIORITY APPLN. INFO.: JP 1985-78283 A 19850415
JP 1985-237695 A 19851025
OTHER SOURCE(S): CASREACT 106:149471; MARPAT 106:149471
AB Nucleoside-phospholipid conjugates R1OCH2CH(OR2)CH2OP(O)(OH)ONs (R1, R2 = fatty acyl; Ns = nucleoside analog) with the title activities are prepared by reaction of an L-glycerophospholipid with a nucleoside in the presence of phospholipase D. For example, 5-fluorouridine in acetate buffer CaCl2

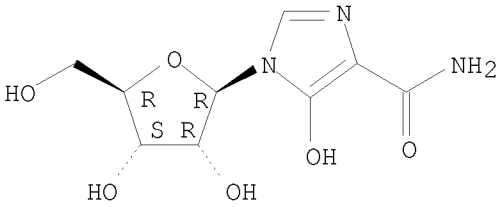
was mixed with Streptomyces phospholipase D-P and a CHCl3 solution of dipalmitoylphosphatidylcholine and the product was purified by solvent extraction and silica gel flash column chromatog. This compound administered 5 + at 30 mg/kg/dose (route not specified) to mice with P-388 leukemia, increased the lifespan by 206.3%.

IT 50924-49-7, Bredinin
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phospholipids)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 13 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1987:628573 CAPLUS

DOCUMENT NUMBER: 107:228573

ORIGINAL REFERENCE NO.: 107:36515a,36518a

TITLE: Synthesis of bredinin 5'-alkylphosphates involving photochemical manipulation of the imidazole moiety, and their antitumor activities

AUTHOR(S): Shuto, Satoshi; Itoh, Hiromichi; Endo, Eriko; Fukukawa, Kiyofumi; Tsujino, Masatoshi; Ueda, Tohru

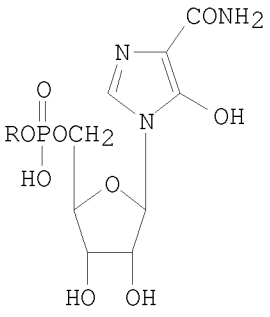
CORPORATE SOURCE: Res. Lab., Toyo Jozo Co., Ltd., Shizuoka, 410-23, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (1987), 35(8), 3523-6
CODEN: CPBTAL; ISSN: 0009-2363

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



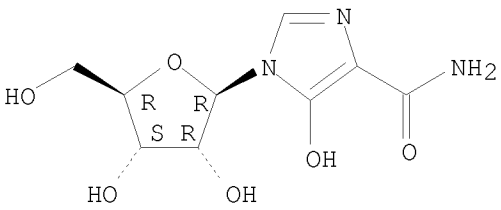
I, R=oleyl

II, R=cetyl

AB Bredinin 5'-oleyl and 5'-cetyl phosphates (I and II), prepared from 1-β-D-ribofuranosyl-5-aminoimidazole-4-carboxamide via a photochem. ring-opening reaction of the imidazole moiety, showed remarkable antitumor effects against various transplantable mouse

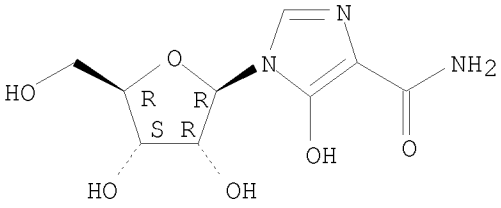
tumors, and were clearly superior to bredinin.
IT 50924-49-7, Bredinin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor activity of, alkyl phosphates in relation to)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 14 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1975:137664 CAPLUS
DOCUMENT NUMBER: 82:137664
ORIGINAL REFERENCE NO.: 82:22019a,22022a
TITLE: Studies on bredinin. I. Isolation, characterization, and biological properties
AUTHOR(S): Mizuno, Kimio; Tsujino, Masatoshi; Takada, Masaki; Hayashi, Mitsuo; Atsumi, Kiyoo; Asano, Katsumi; Matsuda, Tetsuo
CORPORATE SOURCE: Res. Lab., Toyo Jozo Co., Ltd., Ohito, Japan
SOURCE: Journal of Antibiotics (1974), 27(10), 775-82
CODEN: JANTAJ; ISSN: 0021-8820
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Bredinin (I) is a novel imidazole nucleoside with an immunosuppressive activity. It was isolated from the culture filtrate of Eupenicillium brefeldianum M-2166 by means of ion-exchange or partition chromatog. I showed selective cytotoxicity against L5178y cells derived from malignant lymphoma of the mouse. As an immunosuppressant, it had favorable characteristics, namely, a potent activity, low acute toxicity, and a slight effect on a decrease of peripheral leukocytes. I inhibited the growth of vaccinia virus but not that of bacteria or fungi except for Candida albicans in vitro. Slight prolongation in the survival period of mice inoculated with lymphatic leukemia L1210 was observed by i.p. injection of I, however, it was not effective on P388 leukemia or Ehrlich ascites tumor.
IT 50924-49-7
RL: BIOL (Biological study)
(a new immunosuppressant)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.

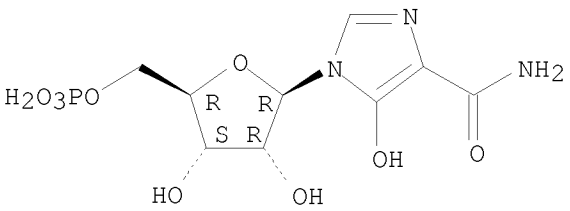


L16 ANSWER 15 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:400211 CAPLUS
DOCUMENT NUMBER: 113:211
ORIGINAL REFERENCE NO.: 113:39a,42a
TITLE: Two distinct target sites on IMP dehydrogenase in chemotherapy
AUTHOR(S): Yamada, Yasukazu; Natsumeda, Yutaka; Yamaji, Yasufumi; Weber, George
CORPORATE SOURCE: Sch. Med., Indiana Univ., Indianapolis, IN, 46223, USA
SOURCE: Advances in Experimental Medicine and Biology (1989), 253B(Purine Pyrimidine Metab. Man 6, Pt. B), 57-63
CODEN: AEMBAP; ISSN: 0065-2598
DOCUMENT TYPE: Journal
LANGUAGE: English

AB IMP dehydrogenase (EC 1.1.1.205), the rate-limiting enzyme of de novo GTP biosynthesis, is a sensitive target in anti-cancer and antiviral chemotherapy. The inhibitory mechanisms of ribavirin 5'-monophosphate (RMP), SM-108 nucleotide (bredinin 5'-monophosphate, BMP) and thiazole-4-carboxamide adenine dinucleotide (TAD), the active metabolites of ribavirin, SM-108 and tiazofurin, resp., were investigated in IMP dehydrogenase from rat hepatoma 3924A. Combinations of the drugs with different modes of inhibitory action were tested in hepatoma 3924A cells in culture. The results indicated that 2 distinct ligand sites of IMP dehydrogenase which provide promising drug targets; NADH site for tiazofurin through its active metabolite, TAD, and XMP-IMP site for ribavirin through its metabolite, RMP. A combination of ribavirin and tiazofurin exerted synergistic inhibitions of de novo guanylate synthesis and colony formation in rat hepatoma cells. A combination chemotherapy directed to the 2 sites on IMP dehydrogenase is thus suggested.

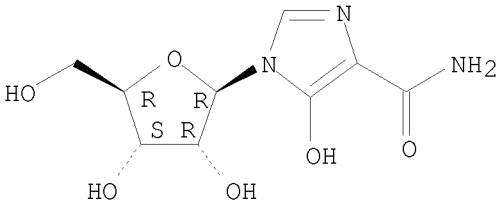
IT 62025-48-3, Bredinin 5'-monophosphate
RL: BIOL (Biological study)
(IMP dehydrogenase ligand site for, as SM-108 metabolite, in combination chemotherapy for hepatoma)
RN 62025-48-3 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-(5-O-phosphono-β-D-ribofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 16 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:400419 CAPLUS
DOCUMENT NUMBER: 117:419
ORIGINAL REFERENCE NO.: 117:75a,78a
TITLE: Modulation of multidrug resistance by immunosuppressive agents: cyclosporin analogs, FK506 and mizoribine
AUTHOR(S): Mizuno, Kimio; Furuhashi, Yoshihito; Misawa, Toshiya; Iwata, Mitsumasa; Kawai, Michiyasu; Kikkawa, Fumitaka; Kano, Takeo; Tomoda, Yutaka
CORPORATE SOURCE: Sch. Med., Nagoya Univ., Nagoya, 466, Japan
SOURCE: Anticancer Research (1992), 12(1), 21-5
CODEN: ANTRD4; ISSN: 0250-7005
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cyclosporin A shows a potent overcoming effect on antitumor multidrug resistance (MDR). Modulating effects of cyclsporine analogs and the immunosuppressive agents FK506 and mizoribine were studied in human multidrug-resistant ovarian cancer cells TAOV/A0.2. The intensity of the overcoming effect of cyclosporin analogs against adriamycin resistance was in the other of cyclosporin D > A > C > H. Cyclosporin D, which has relatively weak immunosuppressive activity, overcame adriamycin resistance in the cancer cells to a remarkable degree. FK506 could also distinctly modulate the adriamycin-resistance. FK506 conferred chemosensitization to adriamycin with increasing intracellular adriamycin accumulation in MDR cells but it was far less compared with the sensitive parent strain. Mizoribine showed no modulation of drug resistance. The modulation was not necessarily accompanied by immunosuppressive activity and the two functions may be based on different mechanisms.
IT 50924-49-7, Mizoribine
RL: BIOL (Biological study)
(adriamycin multidrug resistance in ovary cancer cells modulation by)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



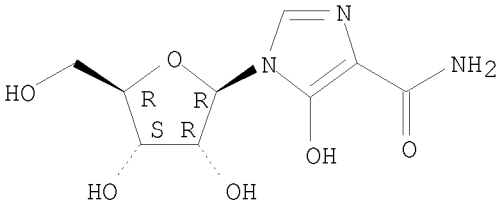
L16 ANSWER 17 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1975:123311 CAPLUS
DOCUMENT NUMBER: 82:123311
ORIGINAL REFERENCE NO.: 82:19727a,19730a
TITLE: Immunosuppressant bredinin by fermentation
INVENTOR(S): Mizuno, Kimio; Ando, Takuji; Takada, Masaki; Hayashi, Mitsuo; Tsujino, Masatoshi; Yoshizawa, Munetoshi; Matsuda, Tetsuo
PATENT ASSIGNEE(S): Toyo Jozo Co., Ltd.
SOURCE: Ger. Offen., 16 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2326916	A1	19741219	DE 1973-2326916	19730523 <--
DE 2326916	C2	19811029		

PRIORITY APPLN. INFO.: DE 1973-2326916 A 19730523
GI For diagram(s), see printed CA Issue.
AB Bredinin (I) was manufactured by fermentation of a common medium with Eupenicillium brefeldianum NRRL 5734 at 26° and purified by chromatog. on silica gel. I had immunosuppressant effects in mice, but no or low antibacterial, antiviral, and neoplasm inhibiting effects.
IT 50924-49-7P
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manufacture of, by Eupenicillium brefeldianum)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 18 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:48609 CAPLUS
DOCUMENT NUMBER: 130:119591
TITLE: Antioxidant enhancement of therapy for hyperproliferative conditions
INVENTOR(S): Chinery, Rebecca; Beauchamp, R. Daniel; Coffey, Robert J.; Medford, Russell M.; Wadsinski, Brian
PATENT ASSIGNEE(S): Atherogenics, Inc., USA
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9901118	A2	19990114	WO 1998-US13750	19980701 <--
WO 9901118	A3	19990422		

W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,

CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2294247	A1	19990114	CA 1998-2294247	19980701	<--
CA 2294247	C	20041026			
AU 9882827	A	19990125	AU 1998-82827	19980701	<--
EP 1019034	A2	20000719	EP 1998-933078	19980701	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002511878	T	20020416	JP 1999-507360	19980701	<--
US 20010049349	A1	20011206	US 2001-779086	20010207	<--
US 7071158	B2	20060704			
AU 2002052761	A	20040108	AU 2002-52761	20020702	
AU 785322	B2	20070118			

PRIORITY APPLN. INFO.:	US 1997-886653	A	19970701
	US 1997-967492	A	19971111
	AU 1998-82827	A	19980701
	US 1998-108609	B1	19980701
	WO 1998-US13750	W	19980701

OTHER SOURCE(S): MARPAT 130:119591

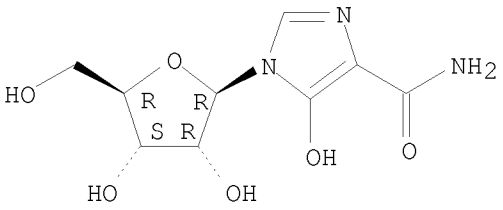
AB A method to enhance the cytotoxic activity of an antineoplastic drug comprises administering an effective amount of the antineoplastic drug to a host exhibiting abnormal cell proliferation in combination with an effective cytotoxicity-increasing amount of an antioxidant. The invention also includes a method to decrease the toxicity to an antineoplastic agent or increase the therapeutic index of an antineoplastic agent administered for the treatment of a solid growth of abnormally proliferating cells, comprising administering an antioxidant prior to, with, or following the antineoplastic treatment.

IT 50924-49-7, Mizoribine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antioxidant enhancement of therapy for hyperproliferative conditions)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 19 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2002:275787 CAPLUS
DOCUMENT NUMBER:	136:304045
TITLE:	Inhibitors of angiogenesis and tumor growth for local and systemic administration
INVENTOR(S):	Singh, Saira Sayed
PATENT ASSIGNEE(S):	Oncopharmaceutical, Inc., USA
SOURCE:	PCT Int. Appl., 36 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028387	A1	20020411	WO 2001-US30986	20011003 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001096558	A5	20020415	AU 2001-96558	20011003 <--
US 20020061303	A1	20020523	US 2001-971062	20011003 <--
US 6696483	B2	20040224		
PRIORITY APPLN. INFO.:			US 2000-237429P P	20001003
			WO 2001-US30986 W	20011003

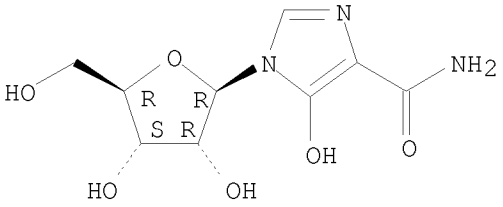
AB The invention provides pharmaceutical formulations and methods for the treatment of individuals suffering from a condition, disease, or disorder that is treatable by the inhibition of angiogenesis. The compns. comprise a Golgi apparatus disturbing agent in a substantially nontoxic amount effective to inhibit angiogenesis in a patient in need of anti-angiogenesis therapy, a solvent, and a pharmaceutically acceptable carrier. In preferred formulations, the Golgi apparatus disturbing agent is brefeldin A.

IT 50924-49-7, Bredinin
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of angiogenesis and tumor growth for local and systemic administration)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 20 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2002:716321 CAPLUS
DOCUMENT NUMBER:	137:246527
TITLE:	Multivalent MHC constructs: Immunoanalysis, diagnosis and therapy
INVENTOR(S):	Winther, Lars; Petersen, Lars Oestergaard; Buus, Soeren; Schoeller, Joergen; Ruub, Erik; Aamellem, Oeystein
PATENT ASSIGNEE(S):	Dako A/S, Den.; Dynal Biotech Asa
SOURCE:	PCT Int. Appl., 304 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002072631	A2	20020919	WO 2002-DK169	20020313 <--
WO 2002072631	A3	20031106		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2440773	A1	20020919	CA 2002-2440773	20020313 <--
AU 2002240818	A1	20020924	AU 2002-240818	20020313 <--
AU 2002240818	B2	20080619		
EP 1377609	A2	20040107	EP 2002-706685	20020313
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005500257	T	20050106	JP 2002-571544	20020313
NO 2003004020	A	20031106	NO 2003-4020	20030911
AU 2008202862	A1	20080724	AU 2008-202862	20080630

PRIORITY APPLN. INFO.:		
DK 2001-435	A	20010314
DK 2001-436	A	20010314
DK 2001-441	A	20010314
US 2001-275447P	P	20010314
US 2001-275448P	P	20010314
US 2001-275470P	P	20010314
AU 2002-240818	A3	20020313
WO 2002-DK169	W	20020313

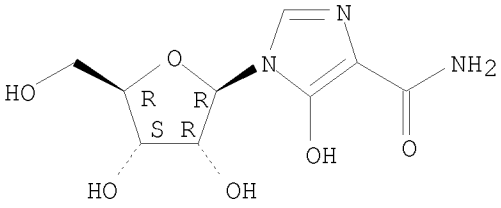
AB The authors disclose MHC mol. constructs (classical and non-classical) conjugated to soluble or insol. carriers wherein the affinity and avidity of the constructs exceed that of comparable MHC tetramers. In one example, the construct is comprised of biotinylated HLA-A2 bound to FITC-labeled streptavidin conjugated to soluble derivatized dextran. The above construct loaded with MART-1 or influenza virus peptides was shown to effect T-cell activation at a lower concentration than. Also comprised by the present invention is the sample-mounted use of MHC mols., MHC mol. multimers, and MHC mol. constructs.

IT 50924-49-7P, Mizoribine
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(of multivalent constructs of MHC antigens for immunoanal., diagnosis, and therapy)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 21 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1986:34310 CAPLUS
DOCUMENT NUMBER: 104:34310
ORIGINAL REFERENCE NO.: 104:5648h,5649a
TITLE: Bredinin 5'-alkyl phosphate esters
PATENT ASSIGNEE(S): Toyo Jozo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
JP 60130596	A	19850712	JP 1983-241562	19831220	<--
JP 03076319	B	19911205			

PRIORITY APPLN. INFO.: JP 1983-241562 19831220
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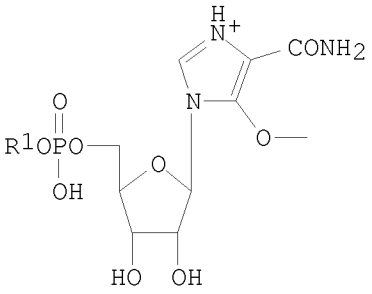
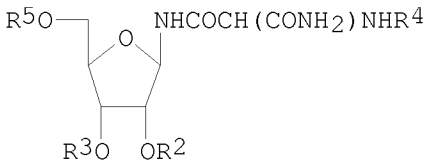
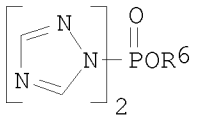


I



II



III

AB The title compound (I, R1 = alkyl, alkenyl) were prepared by reaction of the protected monosaccharide derivs. II (R2, R3, R4 = protecting group; R5 = H) with the phosphoric acid ditriazolide III (R6 = protected group), treatment of the phosphorylated products with R1OH, and cyclization of the imidazole ring and deprotection of the resulting II [R5 = R1OP(O)(OR6)]. Thus, treatment of ribo-II (R2R3 = Me2C, R4 = R5 = H) with p-ClC6H4OP(O)Cl2 in pyridine/dioxane containing Et3N and 1,2,4-triazole at room temperature for 1 h followed by reaction of the product with oleyl alc. in (dimethylamino)pyridine at room temperature for 1 h gave 59.1% II [R2R3 = Me2C, R4 = CO2CMe3, R5 = p-ClC6H4OP(O)(OQ) where Q = oleyl], deprotection of which followed by treatment with HC(OEt)3 in DMF at 90° for 30 min

gave 76.5% I (R1 = p-ClC6H4) oleyl ester, deprotection of which with pyridine 2-aldoxime and (Me2N)2C:NH at 45° for 3-4 h gave 49.2% ribo-I (R1 = oleyl). Some I prolonged the life of Ehrlich cancer cells-implanted mice by >3.8 days.

L16 ANSWER 22 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:401680 CAPLUS
DOCUMENT NUMBER: 133:38237
TITLE: Formulation with an improved therapeutic range, containing nucleotide synthesis inhibitors
INVENTOR(S): Lindner, Juergen; Haase, Burkhard
PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2000033876	A1	20000615	WO 1999-EP9380	19991201	<--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
DE 19857009	A1	20000615	DE 1998-19857009	19981210	<--
CA 2354266	A1	20000615	CA 1999-2354266	19991201	<--
BR 9916006	A	20010904	BR 1999-16006	19991201	<--
EP 1137438	A1	20011004	EP 1999-961041	19991201	<--
EP 1137438	B1	20020605			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
HU 2001004624	A2	20020429	HU 2001-4624	19991201	<--
HU 2001004624	A3	20021228			
AT 218370	T	20020615	AT 1999-961041	19991201	<--
EE 200100305	A	20020815	EE 2001-305	19991201	<--
JP 2002531525	T	20020924	JP 2000-586366	19991201	<--
PT 1137438	T	20021129	PT 1999-961041	19991201	<--
ES 2178496	T3	20021216	ES 1999-961041	19991201	<--
AU 766810	B2	20031023	AU 2000-17793	19991201	
NZ 511882	A	20031128	NZ 1999-511882	19991201	
SK 284842	B6	20051201	SK 2001-788	19991201	
BG 105548	A	20011231	BG 2001-105548	20010530	<--
NO 2001002719	A	20010601	NO 2001-2719	20010601	<--
HR 2001000429	A1	20020630	HR 2001-429	20010607	<--
MX 2001PA05861	A	20020327	MX 2001-PA5861	20010608	<--
ZA 2001004815	A	20020613	ZA 2001-4815	20010613	<--
IN 2001CN00968	A	20070831	IN 2001-CN968	20010710	
HK 1041598	A1	20050715	HK 2002-103282	20020502	
US 20050255071	A1	20051117	US 2005-178987	20050711	

PRIORITY APPLN. INFO.:			
	DE 1998-19857009	A	19981210
	WO 1999-EP9380	W	19991201
	US 1999-457596	B1	19991209

OTHER SOURCE(S): MARPAT 133:38237
AB The therapeutic range of nucleotide synthesis inhibitors (NSI) administered to treat immunol. diseases or cancer or for

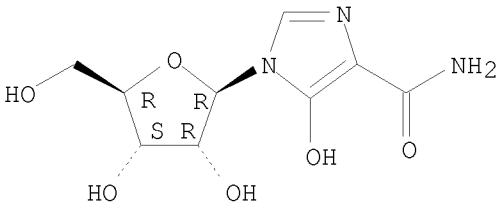
transplantation is increased by (a) interrupting the enterohepatic circulation of NSI (e.g. by orally administering an ion exchanger such as cholestyramine) and/or (b) subsequently administering, after a suitable interval, an antagonist of NSI (e.g. a purine or pyrimidine nucleotide). The action of the agents under (a) and (b) is based on the fact that the desired action of NSI on the immune system is achieved rapidly and is not enhanced by further exposure, whereas side effects of NSI increase during longer residence in the circulation. Thus, rats with adjuvant-induced arthritis were orally administered N-(4-trifluoromethylphenyl)-2-cyano-3-hydroxycrotonamide (2.5 mg/kg/day) and cholestyramine (1000 mg/kg/day) for 17 days to produce a decrease in arthritis index of 92%.

IT 50924-49-7, Mizoribine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulation with improved therapeutic range containing nucleotide synthesis inhibitors)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 23 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1995:569765 CAPLUS

DOCUMENT NUMBER: 123:442

ORIGINAL REFERENCE NO.: 123:91a,94a

TITLE: GTP depletion induced by IMP dehydrogenase inhibitors blocks RNA-primed DNA synthesis

AUTHOR(S): Catapano, Carlo V.; Dayton, Jennifer S.; Mitchell, Beverly S.; Ferandes, Daniel J.

CORPORATE SOURCE: Dep. Exp. Oncol., Med. Univ. South Carolina, Charleston, SC, 29425, USA

SOURCE: Molecular Pharmacology (1995), 47(5), 948-55
CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Inhibitors of IMP dehydrogenase (EC 1.2.1.14), including mizoribine (Bredinin) and mycophenolic acid, have significant antitumor and immunosuppressive activities. Studies were aimed at determining the mechanism by which intracellular GTP depletion induced by these agents results in inhibition of DNA synthesis. Incubation of human CEM leukemia cells for 2 h with IC50 concns. of either mizoribine (4 μM) or mycophenolic acid (0.5 μM) reduced cellular GTP levels an average of 68% or 58%, resp., compared with the levels in control cells. Under similar conditions, mizoribine and mycophenolic acid decreased the amount of [3H]adenosine incorporated into primer RNA by 75% and 70%, resp., relative to the untreated controls, but

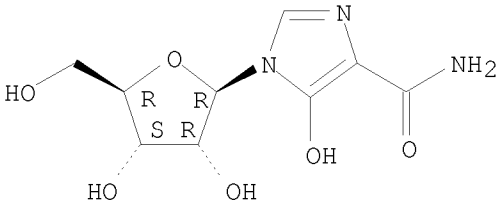
had no significant effect on total RNA synthesis. Repletion of the guanine nucleotide pools by coincubation of CEM cells with guanosine plus 8-aminoguanosine prevented both the inhibition of primer RNA synthesis and the inhibition of tumor cell growth induced by these agents. Addnl. studies demonstrated that GTP depletion alone was capable of directly inducing inhibition of primer RNA synthesis. Primer RNA synthesis was inhibited an average of 84% in whole-cell lysates that lacked GTP but contained all remaining ribo- and deoxyribonucleoside triphosphates. On an M13 DNA template, RNA-primed DNA synthesis catalyzed by the purified complex of DNA primase (EC 2.7.7.6) and DNA polymerase α (EC 2.7.7.7) was decreased an average of 70% in the absence of GTP, compared with synthesis in the presence of 0.5 mM GTP. These results provide evidence that mizoribine and mycophenolic acid inhibit DNA replication by inducing GTP depletion, which suppresses the synthesis of RNA-primed DNA intermediates.

IT 50924-49-7, Mizoribine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(GTP depletion induced by IMP dehydrogenase inhibitors blocks RNA-primed DNA synthesis)

RN 50924-49-7 CAPLUS

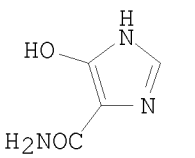
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 24 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1983:231 CAPLUS
DOCUMENT NUMBER: 98:231
ORIGINAL REFERENCE NO.: 98:43a,46a
TITLE: Adenine phosphoribosyltransferase deficiency in cultured mouse mammary tumor FM3A cells resistant to 4-carbamoylimidazolium-5-olate
AUTHOR(S): Koyama, Hideki; Kodama, Hiroaki
CORPORATE SOURCE: Cancer Inst., Jpn. Found. Cancer Res., Tokyo, 170, Japan
SOURCE: Cancer Research (1982), 42(10), 4210-14
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB 4-carbamoylimidazolium-5-olate (CIO) (I) [56973-26-3], the aglycon of the nucleoside antibiotic bredinin, exhibited potent cytotoxic effects on subclonal line F28-7 of C3H mouse mammary carcinoma FM3A cells in culture. Eleven cell lines resistant to CIO were isolated from wild-type F28-7 cells mutated with N-methyl-N'-nitro-N-nitrosoguanidine. These resistant (cior) lines were 160-400-fold less sensitive to CIO than were the wild-type cells and inherited the resistant phenotype during subculture for >3 mo in drug-free medium. They were cross-resistant to an adenine analog, 2,6-diaminopurine, while 2,6-diaminopurine-resistant lines isolated independently were cross-resistant to CIO. None of the cior lines tested was able to form colonies in agar medium containing azaserine and adenine, nor were they able to incorporate tritiated adenine into the macromol. fraction, indicating that they could not utilize exogenous adenine for growth. Enzyme assays using cell-free exts. revealed that all the cior lines had undetectable levels of adenine phosphoribosyltransferase (EC 2.4.2.7) [9027-80-9] activity, but all, except one, had normal levels of hypoxanthine-guanine phosphoribosyltransferase (EC 2.4.2.8) [9016-12-0] and adenosine kinase (EC 2.7.1.20) [9027-72-9] activities. The CIO resistance in these lines is attributable to deficient adenine phosphoribosyltransferase activity, and therefore CIO is activated by this enzyme to form a cytotoxic nucleotide within the drug-sensitive cells.

L16 ANSWER 25 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1991:177772 CAPLUS
DOCUMENT NUMBER: 114:177772
ORIGINAL REFERENCE NO.: 114:29759a,29762a
TITLE: Chemosensitivity test using subrenal capsule assays. 1. Experimental evaluation
AUTHOR(S): Tada, Atsuhiko
CORPORATE SOURCE: Med. Sch., Okayama Univ., Okayama, 700, Japan
SOURCE: Okayama Igakkai Zasshi (1990), 102(11/12), 1287-97
CODEN: OIZAAV; ISSN: 0030-1558
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB New chemosensitivity test using a subrenal capsule assay (SRC) was evaluated. The effects of various immunosuppressants, cyclosporin A (CSA), cyclophosphamide, whole body irradiation, and Bredinin, were studied using human small cell lung cancer cell line (SBC-3) serially transplanted in nude mice. A significant degree of host cell infiltration was seen in tumor fragments implanted under the renal capsule of immunocompetent mice. Treatment with immunosuppressants effectively suppressed the host immune reaction. The most effective immunosuppressant was CSA at 60 mg/kg. The antitumor activities of cisplatin, mitomycin C, etoposide, adriamycin, cyclophosphamide, and vincristine against SBC-3 were compared with SRC and clonogenic assays. SRC was performed using mice administered CSA 60 mg/kg. Chemotherapeutic agents were administered on day 1 and antitumor activities were evaluated on day 6 after implantation. These assays were well-correlated except with vincristine.

L16 ANSWER 26 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:207807 CAPLUS
DOCUMENT NUMBER: 116:207807
ORIGINAL REFERENCE NO.: 116:35003a,35006a
TITLE: Pharmaceuticals containing 4-carbamoyl-1-β-D-ribofuranosyl imidazolium-5-olate for prevention or treatment of HTLV-I-associated myelopathy
INVENTOR(S): Osame, Mitsuhiro; Nomoto, Masahiro

PATENT ASSIGNEE(S): Toyo Jozo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04026626	A	19920129	JP 1990-132071	19900522 <--

PRIORITY APPLN. INFO.: JP 1990-132071 19900522

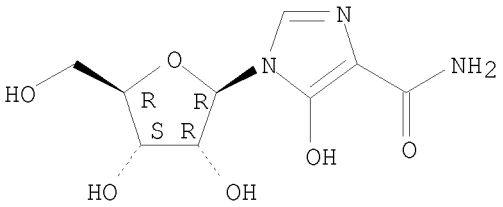
AB Pharmaceuticals for prevention or treatment of HTLV-I (human T-cell lymphotropic virus type I)-associated myelopathy, contain 4-carbamoyl-1-β-D-ribofuranosyl imidazolium-5-olate (mizoribine) as an active ingredient, which are safe and useful for progress prevention and improvement of moving difficulty in HTLV-I-associated myelopathy. Mizoribine at 100-300 mg/day p.o. improved moving difficulty in HTLV-I-associated myelopathy patients. A tablet was formulated containing I 50, lactose anhydride 126, crystalline cellulose 20, CMC-Ca 10, and Mg stearate 2 mg.

IT 50924-49-7, Mizoribine
RL: BIOL (Biological study)
(for treatment of human T-cell lymphotropic virus type I-associated myelopathy)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 27 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:11209 CAPLUS
DOCUMENT NUMBER: 116:11209
ORIGINAL REFERENCE NO.: 116:1982h,1983a
TITLE: Anhydrous crystals of 4-carbamoyl-1-β-D-ribofuranosyl imidazolium-5-oleate
INVENTOR(S): Ozeki, Shinji; Nakatsugawa, Shinichi
PATENT ASSIGNEE(S): Toyo Jozo Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 428879	A2	19910529	EP 1990-120255	19901022 <--
EP 428879	A3	19910807		

EP 428879	B1	19960313			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
JP 03157393	A	19910705	JP 1989-291078	19891110	<--
JP 06015556	B	19940302			
AT 135364	T	19960315	AT 1990-120255	19901022	<--
CA 2028416	A1	19910511	CA 1990-2028416	19901024	<--
CA 2028416	C	19990907			
AU 9064939	A	19910516	AU 1990-64939	19901024	<--
AU 631256	B2	19921119			
US 5442051	A	19950815	US 1994-231011	19940421	<--

PRIORITY APPLN. INFO.:	JP 1989-291078	A	19891110
	US 1990-600617	B1	19901022
	US 1993-61764	B1	19930211

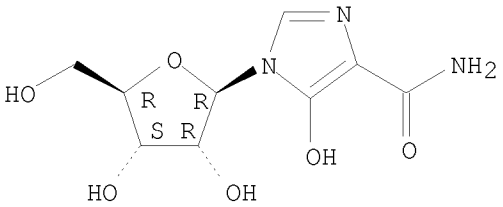
AB Antitumor (no data) 4-carbamoyl-1-β-D-ribofuranosylimidazolium-5-oleate crystals containing ≤ 0.5 weight% H2O and having specific IR spectrum absorption peaks in the neighborhoods of 3580, 1852, 1630, 1575, and 1554 cm-1, are prepared A suspension of 5.0 g purified mizoribine monohydrate crystals containing 6-7% H2O in 50 mL anhydrous MeOH was refluxed in a boiling water bath for 60 min and then cooled in ice cold water for 60 min to give a crystalline precipitate, which was dried overnight at 40° in vacuo to give 4.61 g anhydrous mizoribine crystals containing 0.11% H2O. These crystals remained unchanged after warming at 60° for 24 h in a sealed tube whereas mizoribine monohydrate crystals turned into dark green color.

IT 50924-49-7P
RL: PREP (Preparation)
(anhydrous crystals, preparation of, for pharmaceutical preparation)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 28 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	1990:400264 CAPLUS
DOCUMENT NUMBER:	113:264
ORIGINAL REFERENCE NO.:	113:51a,54a
TITLE:	Studies on the inhibitory effects of immunosuppressive agents and immunomodulating agents on bone resorption of mouse calvaria
AUTHOR(S):	Sasagawa, Kazuko
CORPORATE SOURCE:	Sch. Med., St. Marianna Univ., Kawasaki, 213, Japan
SOURCE:	Sei Marianna Ika Daigaku Zasshi (1989), 27(2), 433-42 CODEN: SMIZDS; ISSN: 0387-2289
DOCUMENT TYPE:	Journal
LANGUAGE:	Japanese

AB The effects of the immunosuppressive agents, cyclosporin A and mizoribine, and the immunomodulating agents, lobenzarit and traxanox, on bone resorption were investigated using neonatal mouse

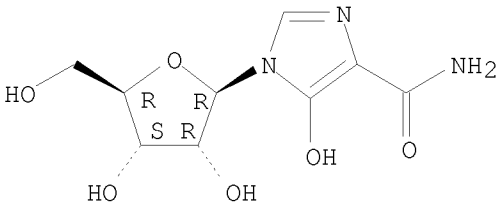
calvariae labeled with 45Ca. As stimulators of bone resorption, bovine parathyroid hormone (PTH), lipopolysaccharide (LPS), interleukin-1β (IL-1β), and tumor necrosis factor-α (TNF-α) were used. Cyclosporin A, mizoribine, lobenzarit, and traxanox inhibited or tended to inhibit bone resorption stimulated by PTH, LPS, IL-1β, or TNF-α in a dose dependent manner. Basal bone resorption was inhibited by immunosuppressive agents cyclosporin A and mizoribine, while immunomodulating agents lobenzarit and traxanox failed to inhibit basal bone resorption. Removal of lobenzarit from the culture medium resulted in the recovery of bone resorptive activity. Thus, the inhibitory effect of an immunomodulating agents on bone resorption is reversible and nonselective. Also, immunomodulating and immunosuppressive agents could affect bone resorption by different mechanisms.

IT 50924-49-7, Mizoribine
RL: BIOL (Biological study)
(bone resorption inhibition by)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 29 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1986:141874 CAPLUS

DOCUMENT NUMBER: 104:141874

ORIGINAL REFERENCE NO.: 104:22247a,22250a

TITLE: Biochemical mode of cytotoxic action of neplanocin A in L1210 leukemic cells

AUTHOR(S): Inaba, Makoto; Nagashima, Kyoko; Tsukagoshi, Shigeru; Sakurai, Yoshio

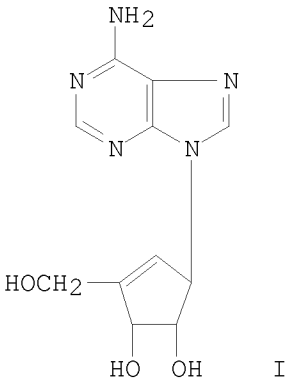
CORPORATE SOURCE: Cancer Chemother. Cent., Jpn. Found. Cancer Res., Tokyo, 170, Japan

SOURCE: Cancer Research (1986), 46(3), 1063-7
CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB Neplanocin A (I) [72877-50-0], a novel antitumor antibiotic, was investigated to determine the biochem. mode(s) of its cytotoxic action. Both sublines of L1210 and P388 leukemia resistant to neplanocin A were cross-resistant in vitro to bredinin and 9-β-D-arabinofuranosyladenine, which have been reported to be activated by adenosine kinase. The adenosine kinase [9027-72-9] activity was markedly reduced in the resistant sublines as compared with that of the resp. sensitive lines. Furthermore, neplanocin A competitively inhibited the phosphorylation reaction of adenosine in a cell-free system. Apparently, neplanocin A is activated by adenosine kinase. Regarding the target site for neplanocin A, the antibiotic suppressed RNA synthesis to a significantly greater extent than DNA synthesis. This RNA-preferential effect is unique among common antimetabolic antitumor agents.

L16 ANSWER 30 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:846523 CAPLUS
DOCUMENT NUMBER: 123:256538
ORIGINAL REFERENCE NO.: 123:45883a,45886a
TITLE: Preparation of carbocyclic and heterocyclic fused-ring quinolinecarboxylic acid immunosuppressive agents
INVENTOR(S): Magolda, Ronald Louis; Pitts, William John; Jacobson, Irina Cipora; Behrens, Carl Henry; Orwat, Michael James; Batt, Douglas Guy
PATENT ASSIGNEE(S): Du Pont Merck Pharmaceutical Co., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9506640	A1	19950309	WO 1994-US9463	19940826 <--
W: AU, BR, CA, CN, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SK				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5428040	A	19950627	US 1993-114712	19930831 <--
CA 2170349	A1	19950309	CA 1994-2170349	19940826 <--
AU 9476358	A	19950322	AU 1994-76358	19940826 <--
AU 690140	B2	19980423		
EP 716652	A1	19960619	EP 1994-926555	19940826 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 74585	A2	19970128	HU 1996-501	19940826 <--
JP 09501442	T	19970210	JP 1995-508162	19940826 <--
RU 2133740	C1	19990727	RU 1996-107400	19940826 <--

IL 110821	A	19970415	IL 1994-110821		19940830 <--
ZA 9406658	A	19960229	ZA 1994-6658		19940831 <--
US 5639759	A	19970617	US 1995-411251		19950327 <--
FI 9600933	A	19960228	FI 1996-933		19960228 <--
NO 9600811	A	19960429	NO 1996-811		19960228 <--
US 5874441	A	19990223	US 1997-820222		19970318 <--
US 6110910	A	20000829	US 1998-195366		19981118 <--
PRIORITY APPLN. INFO.:			US 1993-114712	A	19930831
			WO 1994-US9463	W	19940826
			US 1995-411251	A3	19950327
			US 1997-820222	A3	19970318

OTHER SOURCE(S): MARPAT 123:256538
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

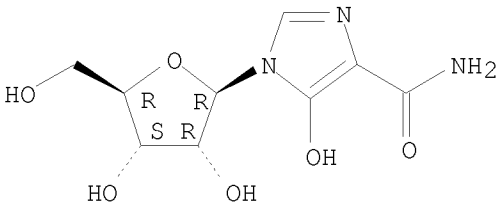
AB The title compds. [I, II; R1, R2 = H, Cl, Br, CF3, alkyl; R3 = Ph, PhO, PhS (un)substituted PhNH, heterocyclyl, etc.; X = YCH2, CH2Y, CH2CH2Y, YCH2CH2, etc.; Y = (un)substituted CH2, O, S, (un)substituted NH; Z1-Z3 = N, (un)substituted CH] (e.g., I; R1 = 6-F, R2 = H, R3 = 4-MeC6H4, X = CH2CH2, Z1-Z3 = CH) [III; Q1, Q2 = S, (un)substituted NH, (un)substituted CH] (IV; Q3, Q4 = N, C; R11 = H, F, Cl, Br, CF3, alkyl), useful as immunosuppressants for the treatment of organ transplantation rejection, graft vs. host diseases, autoimmune diseases, cancer, chronic inflammatory diseases, etc., are prepared and I-, II-, III-, and IV-containing formulations presented.

IT 50924-49-7, Mizoribine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of carbocyclic and heterocyclic fused-ring quinolinecarboxylic acid immunosuppressive agents from)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 31 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

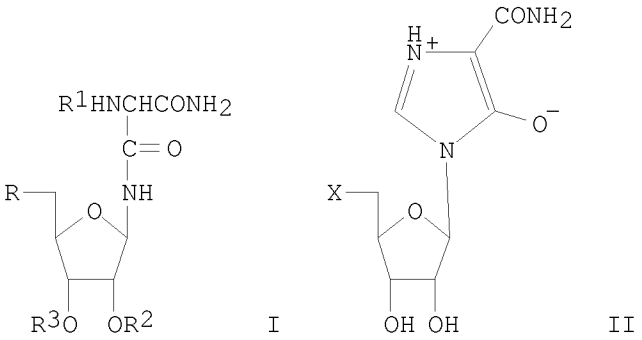
ACCESSION NUMBER:	1986:225187 CAPLUS
DOCUMENT NUMBER:	104:225187
ORIGINAL REFERENCE NO.:	104:35735a,35738a
TITLE:	5'-Halo-5'-deoxybredinins
INVENTOR(S):	Fukukawa, Seishi; Hirano, Takao; Shuto, Satoshi
PATENT ASSIGNEE(S):	Toyo Jozo Co., Ltd., Japan
SOURCE:	Jpn. Kokai Tokkyo Koho, 8 pp. CODEN: JKXXAF
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 60169494	A	19850902	JP 1984-26755	19840214 <--
JP 05010359	B	19930209		

PRIORITY APPLN. INFO.: JP 1984-26755 19840214

GI

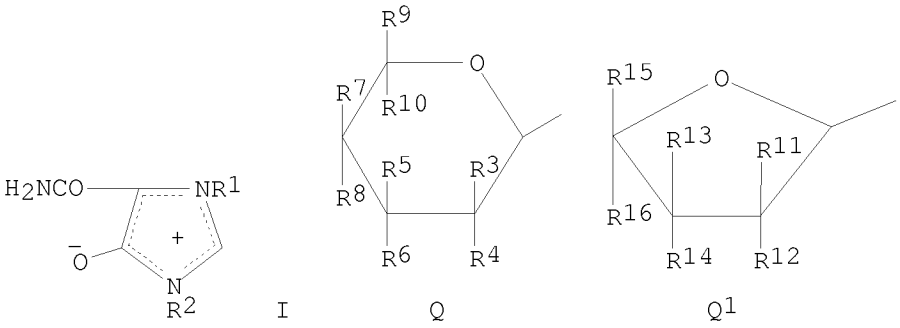


AB I (R = OH; R1 = NH2-protective group; R2,R3 = OH-protective group) were halogenated to give I (R = halo, R1 = NH2-protective group; R2,R3 = OH-protective group), which was deprotected at the site of NH2 (and OH), then cyclized (and deprotected at the site of OH) to give II (X = halo), useful as neoplasm inhibitors. Thus, I (R = OH, R1 = H, R2R3 = isopropylidene) was heated with tert-Bu S-4-dimethylpyrimidin-2-ylthiol carbonate in dioxane containing Et3N at 50° overnight to give 77% I (R = OH, R1 = tert-butoxycarbonyl, R2R3 = isopropylidene) (III). III was treated with methanesulfonyl chloride at room temperature for 3 h and the product refluxed with LiCl in EtCOMe for 6 h to give 73% I (R = Cl, R1 = tert-butoxycarbonyl, R2R3 = isopropylidene), which was deprotected to give I (R = Cl, R1 = R2 = R3 = H) (IV). Heating IV with HC(OEt)3 in DMF at 90° for 40 min gave 50.9% II (X = Cl), whose i.p. administration to mice transplanted with 2 + 106 cells/animal Ehrlich's ascites carcinoma cells prolonged their lives by 56.2%.

L16 ANSWER 32 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1984:571658 CAPLUS
DOCUMENT NUMBER: 101:171658
ORIGINAL REFERENCE NO.: 101:25978h,25979a
TITLE: Imidazole nucleosides
PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 59036695	A	19840228	JP 1982-145314	19820820 <--

PRIORITY APPLN. INFO.: JP 1982-145314 19820820
OTHER SOURCE(S): CASREACT 101:171658
GI



I Q Q1

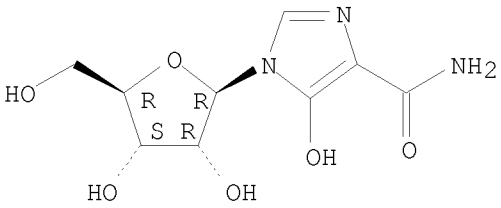
AB Imidazole nucleosides I [R1 = Q (R3,R4 = HO, acyloxy, acetamido, R5,R6 = HO, acyloxy, R7, R8 = HO, acyloxy, R9, R10 = H, Me, HOCH2, acyloxy), Q1 = R11, R12 = HO, acyloxy, R13,R14 = HO, acyloxy, R15, R16 = HOCH2, acyloxymethyl), R2 = H, Q, Q1], useful as neoplasm inhibitors were prepared Thus, 1.271 g 4-carbamoylimidazolium-5-olate, 15 mL hexamethyldisilazane and 25 mL ClCH2CH2Cl were allowed to stand at room temperature, 1.952 g peracetyl-D-glucopyranose and 0.92 mL F3CSO3SiMe3 added, and the resulting solution refluxed 7 h to give 1.280 g I [R1 = Q (R3 = R6 = R7 = R10 = H, R4 = R5 = R8 = AcO; R9 = CH2OAC; R2 = H] which inhibited Lewis carcinoma in mice 52.3% at 200 mg/kg/day dosage for a total of 9 days.

IT 50924-49-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 33 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:624652 CAPLUS

DOCUMENT NUMBER: 131:225481

TITLE: Method for determination of inosine 5'-monophosphate dehydrogenase activity in blood during immunosuppressant therapy

INVENTOR(S): Albrecht, Wolfgang; Bungers, Eva; Martin, Wolfgang; Guserle, Richard

PATENT ASSIGNEE(S): Merckle G.m.b.H., Germany

SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19811313	A1	19990923	DE 1998-19811313	19980316 <--

PRIORITY APPLN. INFO.: DE 1998-19811313 19980316

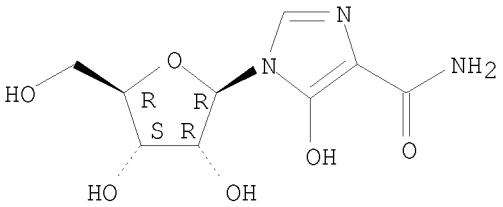
AB The invention concerns the determination of IMP dehydrogenase(IMDPH) activity in blood during cancer therapeutic IMDPH suppression treatment by using IMP substrate and NAD cofactor; and measuring spectrophotometrically one of the reaction components during formation of xanthosine 5'-monophosphate and NADH directly or after cleavage of the xanthosine 5'-monophosphate. Leukocytes are isolated from blood and resuspended in the plasma of the same patient; after sonication, substrate and cofactor are added; the mixture is incubated at 37°C, followed by centrifugation. Using HPLC separation, the quantity of xanthosine 5'-monophosphate is determined at 260 nm. Blood of cancer patients or patients undergoing organ transplantation are assayed by the method. Immunosuppressants used in the therapy are: mycophenolic acid, mycophenolate mofetil, tiazofurine, ribavirin, mizoribine, or VX-497. The invention also concerns a test kit for performing the IMDPH blood assay.

IT 50924-49-7, Mizoribine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for determination of IMP dehydrogenase activity in blood during immunosuppressant therapy)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 34 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:314533 CAPLUS

DOCUMENT NUMBER: 132:334285

TITLE: Preparation of phenyloxoazapropylcycloalkane derivatives and analogs as potassium channel inhibitors

INVENTOR(S): Baker, Robert K.; Chee, Jennifer; Bao, Jianming; Garcia, Maria L.; Kaczorowski, Gregory J.; Kotliar, Andrew; Kayser, Frank; Liu, Chou Juitsai; Miao, Shouwu; Rupprecht, Kathleen M.; Parsons, William H.; Schmalhofer, William A.; Claiborne, Christopher F.; Liverton, Nigel; Claremon, David A.; Thompson, Wayne J.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 243 pp.
CODEN: PIXXD2

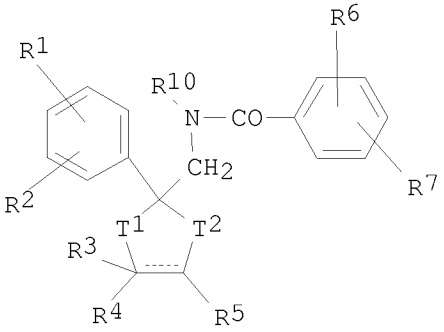
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000025770	A1	20000511	WO 1999-US24949	19991026 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6632836	B1	20031014	US 1999-422143	19991021
CA 2348742	A1	20000511	CA 1999-2348742	19991026 <--
CA 2348742	C	20080729		
EP 1143965	A1	20011017	EP 1999-955159	19991026 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002528490	T	20020903	JP 2000-579211	19991026 <--
AU 764477	B2	20030821	AU 2000-11331	19991026

PRIORITY APPLN. INFO.: US 1998-106416P P 19981030
WO 1999-US24949 W 19991026

OTHER SOURCE(S): MARPAT 132:334285
GI



I

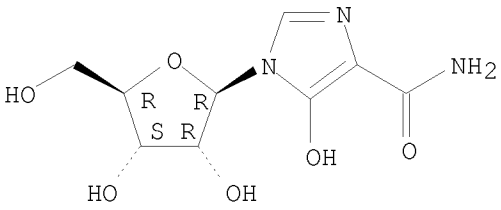
AB The title compds. I [T1 = (CH2)x; T2 = (CH2)y; dotted line indicates a single bond or double bond; x, y = 0 - 2; R1, R2, R6, R7 = halo, hydroxy, alkyl, etc.; R3, R4 = H, cyano, nitro, etc.; further details on R3 and R4 are given; R5 = H, halo, hydroxy, etc.; further details on R3 and R5 are given; R10 = H, etc.], useful as potassium channel inhibitors (no data), are prepared I are useful in the treatment of autoimmune disorders, cardiac arrhythmias (no data), etc. Formulations are given.

IT 50924-49-7, Mizoribine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of phenyloxoazapropylcycloalkane derivs. and a second drug)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

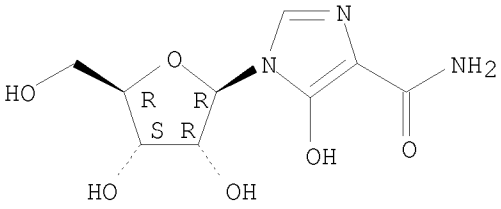
Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 35 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:416729 CAPLUS
DOCUMENT NUMBER: 109:16729
ORIGINAL REFERENCE NO.: 109:2749a,2752a
TITLE: Effect of immunosuppressants on subrenal capsule (SRC) assay as a chemosensitivity test
AUTHOR(S): Irimajiri, Nobuhiro; Haneda, Junichi; Yokoyama, Eiji; Shirakabe, Masaya; Matsumoto, Masamichi; Kusunoki, Tokuro; Utsunomiya, Joji
CORPORATE SOURCE: 2nd Dep. Surg., Hyogo Med. Coll., Nishinomiya, Japan
SOURCE: Gan to Kagaku Ryoho (1988), 15(3), 449-55
CODEN: GTKRDX; ISSN: 0385-0684
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Six-day SRC assay as a chemosensitivity test has an advantage of high predictive rate for clin. response. However, very few viable tumor cells are observed at the end of the assay, making the assay results unreliable. The effect of immunosuppressants on the SRC assay was tested with Walker carcinosarcoma from Wistar rat xenografted under the renal capsule of BDF1 mice. The changes of tumor size, pathol. features and proliferative ability of the tumor xenografted under the renal capsule of mice treated with cyclophosphamide, mizolibine or cyclosporin A were examined Only cyclosporin A treatment maintained the viable tumor cells and proliferative ability of the tumor grafted under the renal capsule 21 days after transplantation. In order to compare the original 6-day SRC assay developed by Bogden et al., immunosuppressants were applied to the 6-day assay. The results suggested that cyclosporin A and mizolibine increase tumor sensitivity in 6-day SRC assay.
IT 50924-49-7
RL: BIOL (Biological study)
(immunosuppression by, during subrenal capsule assay for chemosensitivity evaluation)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 36 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:695812 CAPLUS
DOCUMENT NUMBER: 137:231368
TITLE: Anti-integrin αvβ3 antibodies and immunomodulatory agents for preventing or treating inflammatory or autoimmune disorders
INVENTOR(S): Dingivan, Christine; Wilder, Ronald
PATENT ASSIGNEE(S): Medimmune, Inc., USA
SOURCE: PCT Int. Appl., 193 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070007	A1	20020912	WO 2002-US6679	20020304 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2439852	A1	20020912	CA 2002-2439852	20020304 <--
AU 2002306651	A1	20020919	AU 2002-306651	20020304 <--
AU 2002306651	B2	20071213		
AU 2002306651	B9	20080131		
US 20020168360	A1	20021114	US 2002-91236	20020304 <--
WO 2002098370	A2	20021212	WO 2002-US22273	20020304 <--
WO 2002098370	A3	20031030		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002322478	A1	20021216	AU 2002-322478	20020304 <--
US 20030044406	A1	20030306	US 2002-91313	20020304
US 20030068320	A1	20030410	US 2002-91268	20020304
HU 2003003340	A2	20031229	HU 2003-3340	20020304
EP 1372720	A1	20040102	EP 2002-748394	20020304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1507354	A	20040623	CN 2002-809320	20020304
JP 2004536786	T	20041209	JP 2002-569179	20020304
NZ 528076	A	20050930	NZ 2002-528076	20020304
NO 2003003862	A	20031031	NO 2003-3862	20030901
MX 2003PA07878	A	20040708	MX 2003-PA7878	20030902
ZA 2003006845	A	20050302	ZA 2003-6845	20030902
IN 2003CN01544	A	20051125	IN 2003-CN1544	20030930
US 20070025990	A1	20070201	US 2006-541237	20060929
AU 2008201162	A1	20080403	AU 2008-201162	20080312

PRIORITY APPLN. INFO.:

US 2001-273098P	P	20010302
US 2001-316321P	P	20010831
US 2001-346918P	P	20011019
US 2002-358424P	P	20020219
AU 2002-306651	A3	20020304
US 2002-91268	B1	20020304
WO 2002-US22273	W	20020304
WO 2002-US6679	W	20020304

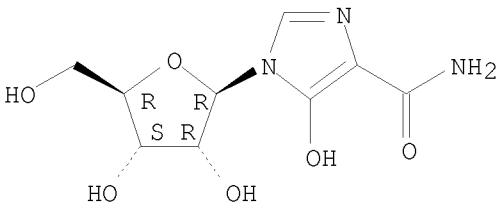
AB The present invention provides to methods of preventing, treating or ameliorating one or more symptoms associated with an autoimmune or inflammatory disorder utilizing combinatorial therapy. In particular, the present invention provides methods of preventing, treating, or ameliorating one or more symptoms associated with an autoimmune or inflammatory disorder comprising administering to a subject in need thereof one or more integrin αVβ3 antagonists and at least one other prophylactic or therapeutic agent. The present invention also provides compns. and articles of manufacture for use in preventing, treating or ameliorating one or more symptoms associated with an autoimmune or inflammatory disorder.

IT 50924-49-7, Mizoribine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-integrin αvβ3 antibodies and immunomodulatory agents for preventing or treating inflammatory or autoimmune disorders)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 37 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1979:483122 CAPLUS

DOCUMENT NUMBER: 91:83122

ORIGINAL REFERENCE NO.: 91:13338h,13339a

TITLE: Induction of sister chromatid exchanges in Chinese hamster cells by antitumor agents and its relation to chromosome aberrations

AUTHOR(S): Sono, Akira; Sakaguchi, Kengo

CORPORATE SOURCE: Res. Lab., Toyo Jozo Co. Ltd., Shizuoka, Japan

SOURCE: Cell Structure and Function (1978), 3(4), 341-7
CODEN: CSFUDY; ISSN: 0386-7196

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Various antitumor agents were used to investigate the induction of sister chromatid exchanges (SCEs), one of the most sensitive tests for detecting the effects of mutagenic carcinogens. Antimetabolites of nucleic acid synthesis and inhibitors of protein synthesis were tested on Chinese hamster cells in vitro. These substances increased the frequency of SCEs even after a 1-h exposure and during the limited stage of the last cell

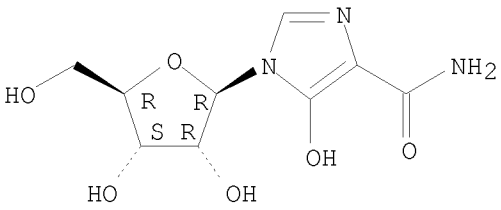
division cycle before fixation. The response curves of SCEs and chromosome aberrations were somewhat similar, but seemed to fluctuate independently of each other; chromosome breaks and gaps induced by the agents were not necessarily associated with SCEs at the breakpoints. Possible relations between SCE formation and chromosome aberrations are discussed.

IT 50924-49-7
RL: BIOL (Biological study)
(chromatid exchanges and chromosome aberrations from, in animal cells)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 38 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1987:116065 CAPLUS

DOCUMENT NUMBER: 106:116065

ORIGINAL REFERENCE NO.: 106:18913a

TITLE: Synthesis of 5'-phosphatidylnucleosides by phospholipase D-catalyzed transphosphatidylation

AUTHOR(S): Shuto, Satoshi; Ueda, Shigeru; Itoh, Hiromichi; Endo, Eriko; Fukukawa, Kiyofumi; Imamura, Shigeyuki; Tsujino, Masatoshi; Matsuda, Akira; Ueda, Tohru

CORPORATE SOURCE: Res. Lab., Toyo Jozo Co., Ltd., 632-1, Japan

SOURCE: Nucleic Acids Symposium Series (1986), 17(Symp. Nucleic Acids Chem., 14th, 1986), 73-6
CODEN: NACSD8; ISSN: 0261-3166

DOCUMENT TYPE: Journal

LANGUAGE: English

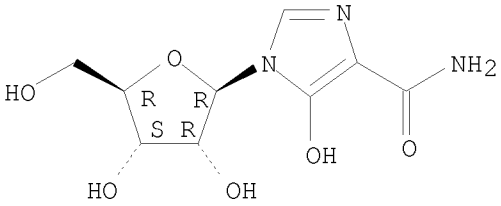
AB Phospholipase D from Streptomyces effectively catalyzed the transfer reaction of the phosphatidyl residue from phosphatidylcholine to the 5'-hydroxyl group of nucleosides. A variety of 5'-phosphatidylnucleosides were prepared by this reaction in high yields. Some of them showed marked antitumor activities in mice.

IT 50924-49-7, Bredinin
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phosphatidylcholines, phospholipase D from Streptomyces in)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

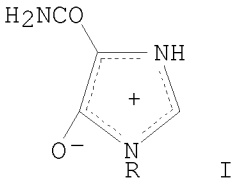
Absolute stereochemistry.



L16 ANSWER 39 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1984:511351 CAPLUS
DOCUMENT NUMBER: 101:111351
ORIGINAL REFERENCE NO.: 101:17021a,17024a
TITLE: 1-Substituted imidazole nucleosides
PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 59031797	A	19840220	JP 1982-143162	19820818 <--

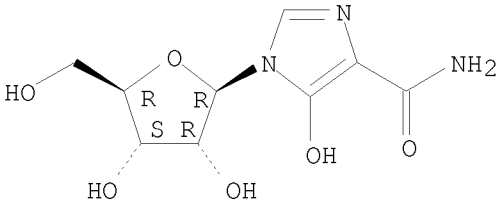
PRIORITY APPLN. INFO.: JP 1982-143162 19820818
OTHER SOURCE(S): CASREACT 101:111351
GI



I

AB Nine 1-substituted imidazole nucleosides I [R = β-D-glucopyranosyl, β-D-galactopyranosyl (Q), β-D-xylofuranosyl, etc.] were prepared by reaction of 4-carbamoylimidazolium-5-olate (II) with R1X (R1 = acylated R; X = halo, alkoxy, alkanoyloxy) in the presence of SnCl4 and condensing agents optionally followed by deacylation. I had immunosuppressive and anticarcinogenic activities (no data). Thus, a mixture of 2.542 g II, 19 mL (Me3Si)2NH, and 25 mg (NH4)2SO2 in xylene was refluxed 2 h, concentrated, the resulting trimethylsilyl derivative dissolved in (CH2Cl)2, 7.807 g peracetyl-D-galactopyranose, 2.11 mL SnCl4, and 0.366 mL trimethylsilyl trifluoromethanesulfonate were added, and the whole was refluxed 2 h to give 6.102 g I (R = tetraacetyl Q). Stirring this (1.372 g) with NaOMe-MeOH 1.5 h at room temperature gave 738 mg I (R = Q).
IT 50924-49-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

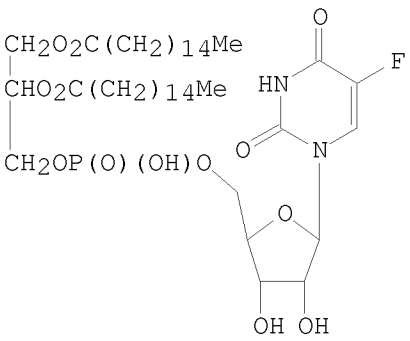
Absolute stereochemistry.



L16 ANSWER 40 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:5741 CAPLUS
DOCUMENT NUMBER: 118:5741
ORIGINAL REFERENCE NO.: 118:1243a,1246a
TITLE: Base exchange reaction with phospholipase D-P in manufacture of anticancer agents
INVENTOR(S): Shuto, Satoshi; Ito, Hiromichi; Fukukawa, Seishi; Sakakibara, Hideo
PATENT ASSIGNEE(S): Toyo Jozo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04211387	A	19920803	JP 1991-39430	19910208 <--

PRIORITY APPLN. INFO.: JP 1991-39430 19910208
OTHER SOURCE(S): MARPAT 118:5741
GI



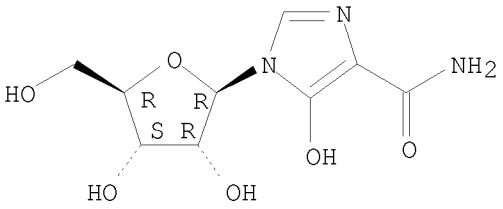
I

AB Phosphatidycholines are incubated with phospholipase D-P in the presence of N-containing alcs. or polyols for base exchange reaction to manufacture novel neoplasm inhibitors. 5-Fluorouridine in CaCl2-containing acetate buffer was incubated with phospholipase D-P of Streptomyces and CHCl3 solution of dipalmitoylphosphatidylcholine at 45° for 3 h to manufacture 50.5% glycerophosphate-5-fluorouridine condensate I. I at 30 mg/kg/day was administered i.p. to P-388 leukemia-bearing mice for 5 days to show 206.3% T/C (treated group/control group) mean survival days. LD50 of I was >150 mg/kg i.p. (no information on test animals).

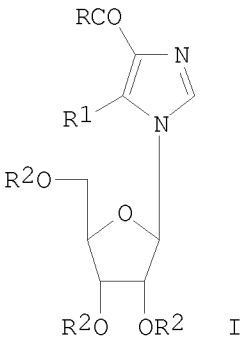
IT 50924-49-7, Bredinin
RL: BIOL (Biological study)

(condensation of, with phosphatidylcholines, with phospholipase D-P)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 41 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1985:488163 CAPLUS
DOCUMENT NUMBER: 103:88163
ORIGINAL REFERENCE NO.: 103:14173a,14176a
TITLE: Synthesis and biological activity of 5-thiobredinin and certain related 5-substituted imidazole-4-carboxamide ribonucleosides
AUTHOR(S): Wood, Steven G.; Upadhya, Krishna G.; Dalley, N. Kent; McKernan, Patricia A.; Canonico, Peter G.; Robins, Roland K.; Revankar, Ganapathi R.
CORPORATE SOURCE: Cancer Res. Cent., Brigham Young Univ., Provo, UT, 84602, USA
SOURCE: Journal of Medicinal Chemistry (1985), 28(9), 1198-203
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 103:88163
GI

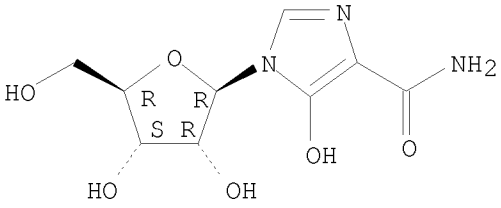


AB Several 5-substituted imidazole-4-carboxamide ribonucleosides were prepared and tested for their biol. activity. Treatment of 5-chloro-1-β-D-ribofuranosylimidazole-4-carboxamide (I, R = H2N, R1 = Cl, R2 = H)(II) with MeSH provided I (R = H2N, R2 = MeS, R2 = H)(III). Similar treatment of II with EtSH or PhCH2SH gave I (R2 = EtS)(IV) and I (R2 = PhCH2S)(V), resp. Oxidation of III and IV with 3-ClC6H4C(O)OOH furnished the corresponding sulfonyl derivs. Reductive cleavage of V with Na naphthalene or Na/NH3 gave I (R = H2N, R1 = HS, R2 = H)(5-

thiobredinin)(VI). Direct treatment of II with NaSH provided an alternate route to VII, the structure of which was established by single-crystal x-ray anal. VI has a zwitterionic structure similar to that of bredinin. Glycosylation of persilylated Et 5(4)-methylimidazole-4(5)-carboxylate with 1-O-acetyl-2,3,5-tri-O-benzoyl-D-ribofuranose in the presence of SnCl4 provided a quant. yield of I (R = EtO, R1 = Me, R2 = Bz)(VII). Debenzoylation of VII with MeOH/NH3 at ambient temperature gave I (R = EtO, R1 = Me, R2 = H). Further ammonolysis of the latter compound or VII at elevated temperature and pressure gave I (R = H2N, R1 = Me, R2 = H). All of these ribonucleosides were tested in Vero cell cultures and in mice against certain viruses. III and V exhibited significant activity against vaccinia virus in vitro. VI failed to exhibit appreciable antiviral or cytostatic activity (against L1210 and P388) in cell culture.

L16 ANSWER 42 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:111701 CAPLUS
DOCUMENT NUMBER: 112:111701
ORIGINAL REFERENCE NO.: 112:18723a,18726a
TITLE: Different inhibitory actions of immunomodulating agents and immunosuppressive agents on bone resorption of mouse calvaria
AUTHOR(S): Sasagawa, Kazuko; Fujibayashi, Shigeru; Okano, Kazutoshi; Nawa, Chieko; Suzuki, Satoshi; Kou, Shosei; Yamada, Yukio; Someya, Kazuhiko
CORPORATE SOURCE: Sch. Med., St. Marianna Univ., Kawasaki, 213, Japan
SOURCE: International Journal of Immunopharmacology (1989), 11(8), 953-9
CODEN: IJIMDS; ISSN: 0192-0561
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The in vitro effects of the immunomodulators lobenzarit and traxanox and a newly synthesized immunosuppressant, mizoribine, as well as cyclosporin A, were studied on bone resorption using neonatal mouse calvariae labeled with 45Ca. As stimulators of bone resorption, bovine parathyroid hormone (PTH), lipopolysaccharide (LPS), interleukin 1β (IL-1β), and tumor necrosis factor-α (TNF-α) were used. Lobenzarit, traxanox, mizoribine, and cyclosporin A inhibited or tended to inhibit bone resorption stimulated by PTH, LPS, IL-1β, or TNF-α in a dose-dependent manner. Basal bone resorption was inhibited by immunosuppressant cyclosporin A or mizoribine, while immunomodulators lobenzarit and traxanox failed to inhibit basal bone resorption. Removal of lobenzarit from the culture medium resulted in the recovery of bone resorptive activity. Thus, the inhibitory effect of immunomodulator on bone resorption is reversible and nonselective. Also, immunomodulators and immunosuppressants may affect bone resorption by different mechanisms.
IT 50924-49-7, Mizoribine
RL: BIOL (Biological study)
(basal and stimulated bone resorption inhibition by)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



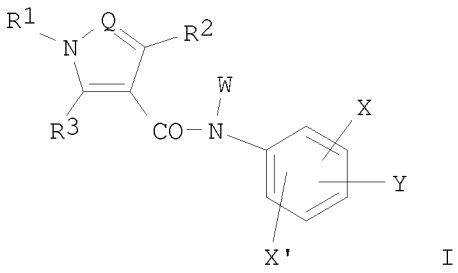
L16 ANSWER 43 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:573775 CAPLUS
DOCUMENT NUMBER: 133:177164
TITLE: Preparation of pyrazolecarboxamides and pyrrolecarboxamides as inhibitors of the proliferation of activated lymphocytes and as remedies for autoimmune disease.
INVENTOR(S): Ushio, Hiroyuki; Ishibuchi, Seigo; Naito, Youichiro; Sugiyama, Naoki; Kawaguchi, Takafumi; Chiba, Kenji; Ohtsuki, Makio; Naka, Yoichi
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 315 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047558	A1	20000817	WO 2000-JP767	20000210 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2362381	A1	20000817	CA 2000-2362381	20000210 <--
NZ 514095	A	20010928	NZ 2000-514095	20000210 <--
EP 1176140	A1	20020130	EP 2000-902925	20000210 <--
EP 1176140	B1	20041229		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008173	A	20021022	BR 2000-8173	20000210 <--
JP 3419395	B2	20030623	JP 2000-598479	20000210
JP 2003176273	A	20030624	JP 2002-375683	20000210
AT 286026	T	20050115	AT 2000-902925	20000210
ES 2234564	T3	20050701	ES 2000-902925	20000210
MX 2001PA08142	A	20030721	MX 2001-PA8142	20010810
US 7015218	B1	20060321	US 2001-913260	20011119

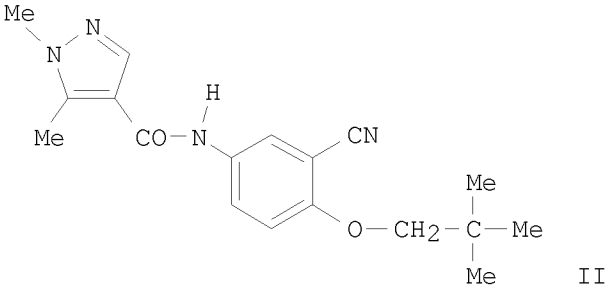
PRIORITY APPLN. INFO.:

JP 1999-33367	A	19990210
JP 1999-198473	A	19990713
JP 2000-598479	A3	20000210
WO 2000-JP767	W	20000210

OTHER SOURCE(S): MARPAT 133:177164
GI



I



II

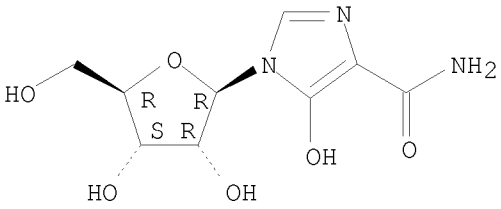
AB The title compds. I [R1 represents substituted aryl, heteroaryl, etc.; R2 and R3 represent each hydrogen, alkyl, halogeno, hydroxy, etc.; Q represents N, CH, etc.; W represents hydrogen, alkyl, hydroxycarbonylalkyl, etc.; X represents halogeno, cyano, nitro, amino, etc.; X' represents hydrogen, halogeno, cyano or nitro; and Y represents alkyl, hydroxy, alkoxy, etc.] are prepared For example, pyrazolecarboxamide derivative II was prepared The title compds. are said to show significant inhibiting activity against the proliferation of activated lymphocytes in in vitro tests. A formulation is given.

IT 50924-49-7, Mizoribine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug combination including pyrazolecarboxamides and pyrrolecarboxamides and other agents)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



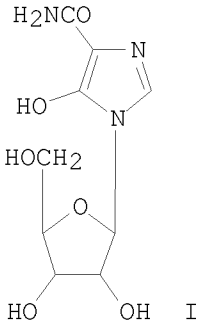
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 44 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1983:40583 CAPLUS
DOCUMENT NUMBER: 98:40583
ORIGINAL REFERENCE NO.: 98:6205a,6208a
TITLE: Antitumor pharmaceuticals
PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 57156418	A	19820927	JP 1981-41109	19810319 <--

PRIORITY APPLN. INFO.: JP 1981-41109 19810319
GI



I

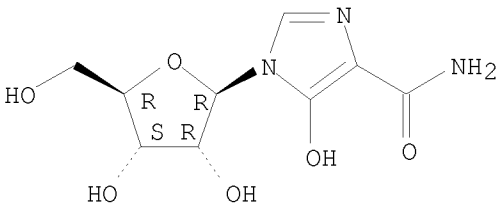
AB Pharmaceuticals containing 4-carbamoyl-1-β-D-ribofuranosylimidazolium-5-olate (I) [50924-49-7] or its salts. are useful as antitumor agents. Thus, tablets were prepared containing I 250, mannitol 200, potato starch 47 and Mg stearate 3 mg. I administered i.p. prolonged the life span of mice with Ehrlich ascites carcinoma.

IT 50924-49-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm inhibitor)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 45 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:389119 CAPLUS
DOCUMENT NUMBER: 129:45285
ORIGINAL REFERENCE NO.: 129:9399a,9402a
TITLE: Inosinate dehydrogenase inhibitors for treatment of restenosis after percutaneous transluminal coronary angioplasty (PTCA)
INVENTOR(S): Ando, Kunio; Tamura, Takezo
PATENT ASSIGNEE(S): Ando, Kunio, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10158191	A	19980616	JP 1996-353400	19961128 <--

PRIORITY APPLN. INFO.: JP 1996-353400 19961128

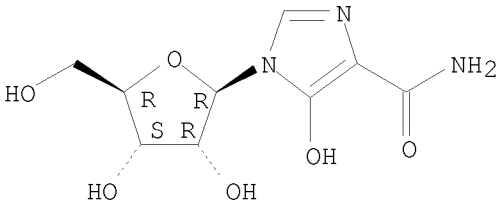
AB Mycophenolic acid (I), mizoribine, etc., are useful for prevention and treatment of restenosis after PTCA, which has been performed in patients with ischemic heart disease. I inhibited formation of glycoprotein and glycolipid of cell surface layer in sarcoma 180 cell.

IT 50924-49-7, Mizoribine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inosinate dehydrogenase inhibitors for treatment of restenosis after percutaneous transluminal coronary angioplasty)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 46 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:147190 CAPLUS
DOCUMENT NUMBER: 128:208915
ORIGINAL REFERENCE NO.: 128:41263a,41266a
TITLE: Methods for the production of protein particles useful for delivery of pharmacological agents
INVENTOR(S): Magdassi, Shlomo; Desai, Neil; Ferreri, Kevin; Soon-Shiong, Patrick
PATENT ASSIGNEE(S): Vivorx Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9807410	A1	19980226	WO 1997-US14661	19970819 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ,

VN, YU
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2263765	A1	19980226	CA 1997-2263765	19970819 <--
AU 9739169	A	19980306	AU 1997-39169	19970819 <--
EP 938299	A1	19990901	EP 1997-936517	19970819 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1683517	A1	20060726	EP 2006-7715	19970819
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

US 1996-23968P	P	19960819
EP 1997-936517	A3	19970819
WO 1997-US14661	W	19970819

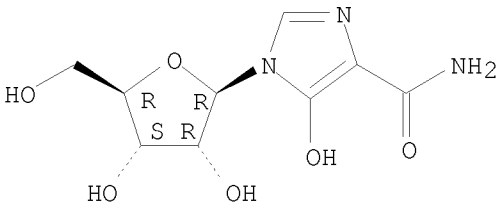
AB A method has been developed for the formation of submicron particles (nanoparticles) by heat-denaturation of proteins (such as human serum albumin) in the presence of multivalent ions (such as calcium). Also provided are novel products produced by the invention method. An appropriate concentration of multivalent ions, within a relatively narrow range of concns., induces the precipitation of protein in the form of colloidal particles, at a temperature which is well below the heat denaturation temperature of the protein (as low as 60 °C for serum albumin). Temps. at which invention method operates are sufficiently low to permit incorporation of other mols. (e.g., by co-precipitation), into submicron particles according to the invention, including compds. which cannot withstand high temps. Invention methods facilitate the production of protein nanoparticles and microparticles containing various mols. (such as nucleic acids, oligonucleotides, polynucleotides, DNA, RNA, polysaccharides, ribozymes, pharmacol. active compds., and the like) useful for therapeutic, diagnostic and other purposes. The addition of multivalent cations serves both to induce precipitation, and to allow linking of neg. charged mols., such as DNA, to the neg. charged protein. Microparticles and nanoparticles were formed from albumin in the presence of CaCL2.

IT 50924-49-7, Mizoribine
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(production of protein particles useful for delivery of pharmacol. agents)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 47 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:695785 CAPLUS

DOCUMENT NUMBER: 137:210973
TITLE: Administration of sleep restorative agents and efficacy of drug therapy
INVENTOR(S): Holman, Andrew
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069974	A1	20020912	WO 2002-US6786	20020305 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002245598	A1	20020919	AU 2002-245598	20020305 <--
US 20020165246	A1	20021107	US 2002-91744	20020305 <--
US 20080089859	A1	20080417	US 2007-736406	20070417

PRIORITY APPLN. INFO.:		
US 2001-273667P	P	20010305
US 2002-91744	B1	20020305
WO 2002-US6786	W	20020305

OTHER SOURCE(S): MARPAT 137:210973

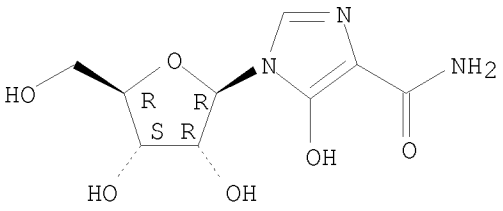
AB The present invention provides methods and compns. for increasing the efficacy of a therapeutic agent administered to a subject. A sleep restorative agent is co-administered to the subject along with the therapeutic agent, whereby the efficacy of the therapeutic agent is increased.

IT 50924-49-7, Mizoribine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(administration of sleep restorative agents and efficacy of drug therapy)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 48 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:695726 CAPLUS

DOCUMENT NUMBER: 137:231367
TITLE: Anti-CD2 antibodies or CD2 antagonists and immunomodulating agents for preventing or treating inflammatory or autoimmune disorders
INVENTOR(S): Dingivan, Christine
PATENT ASSIGNEE(S): Medimmune, Inc., USA
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069904	A2	20020912	WO 2002-US6761	20020304 <--
WO 2002069904	A3	20030220		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002250236	A1	20020919	AU 2002-250236	20020304 <--
AU 2002322478	A1	20021216	AU 2002-322478	20020304 <--
ZA 2003006845	A	20050302	ZA 2003-6845	20030902
US 20070025990	A1	20070201	US 2006-541237	20060929

PRIORITY APPLN. INFO.:		
US 2001-273098P	P	20010302
US 2001-346918P	P	20011019
US 2002-358424P	P	20020219
US 2002-91268	B1	20020304
WO 2002-US22273	W	20020304
WO 2002-US6761	W	20020304

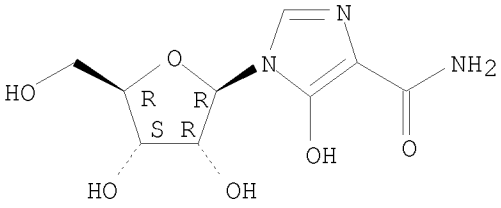
AB The present invention provides to methods of preventing, treating or ameliorating an autoimmune or inflammatory disorder or one or more symptoms thereof utilizing combinatorial therapy. In particular, the present invention provides methods of preventing, treating, or ameliorating an autoimmune or inflammatory disorder or one or more symptoms thereof comprising administering to a subject in need thereof one or more CD2 antagonists and at least one other prophylactic or therapeutic agent. The present invention also provides compns. and articles of manufacture for use in preventing, treating or ameliorating one or more symptoms associated with an autoimmune or inflammatory disorder.

IT 50924-49-7, Mizoribine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-CD2 antibodies or CD2 antagonists and immunomodulating agents for preventing or treating inflammatory or autoimmune disorders)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.

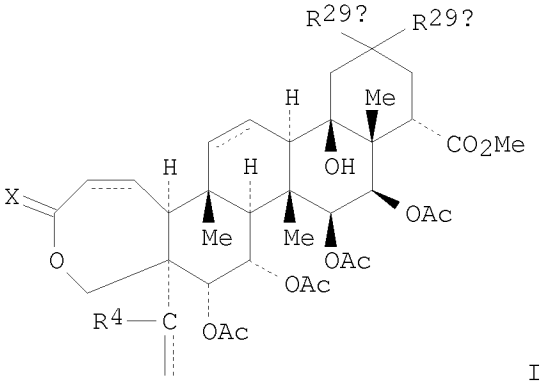


L16 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:405900 CAPLUS
DOCUMENT NUMBER: 127:13451
ORIGINAL REFERENCE NO.: 127:2622h,2623a
TITLE: Triterpene derivatives with immunosuppressant activity, their preparation, and compositions containing them
INVENTOR(S): Baker, Robert K.; Bao, Jianming; Kayser, Frank; Parsons, William H.; Rupprecht, Kathleen M.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA; Baker, Robert K.; Bao, Jianming; Kayser, Frank; Parsons, William H.; Rupprecht, Kathleen M.
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9716068	A1	19970509	WO 1996-US17211	19961028 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2235886	A1	19970509	CA 1996-2235886	19961028 <--
AU 9674781	A	19970522	AU 1996-74781	19961028 <--
AU 712015	B2	19991028		
EP 877554	A1	19981118	EP 1996-937010	19961028 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11514648	T	19991214	JP 1996-517439	19961028 <--

PRIORITY APPLN. INFO.:			
US 1995-8169P	P	19951031	
US 1995-8189P	P	19951031	
GB 1996-3833	A	19960223	
GB 1996-5156	A	19960312	
WO 1996-US17211	W	19961028	

OTHER SOURCE(S): MARPAT 127:13451
GI



I

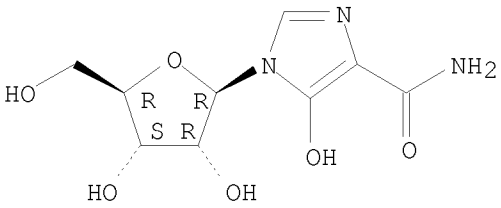
AB Compds. I [X= O, S, NH, or H and R1; a = single bond, double bond when R4 absent; b,c = single bond, double bond; R1, R2 = H, (un)substituted C1-6 alkyl; R4 = absent (a = double bond), H, OH, :O, etc.; R29a, R29b = H, :O, (CH2)sOH, (CH2)sNR1R2, etc.; s = 0, 1] are useful as immunosuppressive agents. Compds. of the invention produce a blockade of the KV1.3 voltage-gated potassium channel. Isolation of compds. from Spachea correa, synthetic preparation of compds., and pharmaceutical compns. are described.

IT 50924-49-7, Mizoribine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triterpene derivs. with immunosuppressant activity, preparation, and (combination) compns.)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 50 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1988:542099 CAPLUS

DOCUMENT NUMBER: 109:142099

ORIGINAL REFERENCE NO.: 109:23443a,23446a

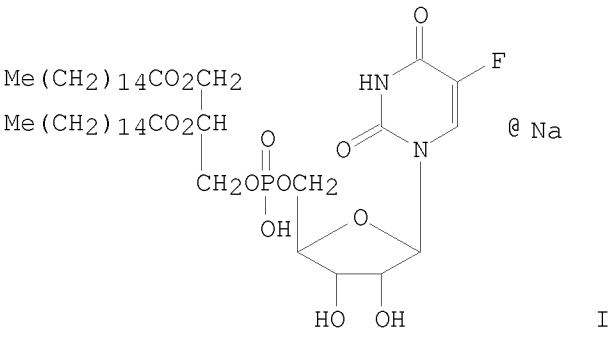
TITLE: A facile enzymic synthesis of 5'-(3-sn-phosphatidyl)nucleosides and their antileukemic activities

AUTHOR(S): Shuto, Satoshi; Ito, Hiromichi; Ueda, Shigeru; Imamura, Shigeyuki; Fukukawa, Kiyofumi; Tsujino, Masatoshi; Matsuda, Akira; Ueda, Toru

CORPORATE SOURCE: Res. Lab., Toyo Jozo Co., Ltd., Shizuoka, 410-23, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (1988), 36(1), 209-17

CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 109:142099
GI

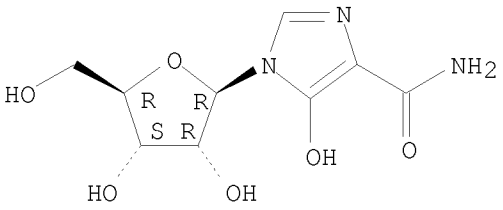


I

AB Phospholipase D from Streptomyces effectively catalyzed the transfer reaction of the phosphatidyl residue from 3-sn-phosphatidylcholine to the 5'-hydroxyl group of nucleosides in a two-phase system. Thus, a variety of 5'-(3-sn-phosphatidyl)nucleosides could be readily prepared in high yields by means of this reaction. Among them, phosphatidyl-FUR (I), phosphatidyl-Ara FC, and phosphatidyl-neplanocin A each produced a significant increase in the life span of mice bearing i.p.-implanted P388 leukemia, being more effective than the parent nucleosides.

IT 50924-49-7, Bredinin
RL: PROC (Process)
(transphosphatidylation of)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

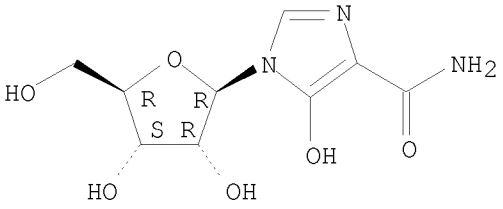
Absolute stereochemistry.



L16 ANSWER 51 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:644928 CAPLUS
DOCUMENT NUMBER: 121:244928
ORIGINAL REFERENCE NO.: 121:44399a,44402a
TITLE: Evaluation of a subrenal capsule assay for sensitivity to anticancer drugs modified by the combination with immunosuppressants
AUTHOR(S): Yokoyama, Eiji; Kusunoki, Tokuro; Utsunomiya, Joji
CORPORATE SOURCE: 2nd Department Surgery, Hyogo College Medicine, Japan
SOURCE: Nippon Gan Chiryo Gakkaishi (1994), 29(7), 936-45
CODEN: NGCJAK; ISSN: 0021-4671

DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Three immunosuppressants (cyclophosphamide - CPM; mizolibine - Br; cyclosporine - Cs) were used in combination with the subrenal capsule assay (SRC assay) reported by Bogden, and the usefulness of the assay was examined on Walker 256 carcino-sarcoma. The results of the assay were compared with the antitumor effect obtained in a rat chemotherapy model to determine the predictability of the antitumor effect. The combination of the immunosuppressants were effective in inhibiting the host response compared to the original SRC assay, and Cs was the most effective immunosuppressant. The highest correlation with the rat chemotherapy model was also obtained by the combination with Cs. In conclusion, the antitumor effectiveness of the drug could be predicted at a high rate of accuracy by the use of Cs in combination with the SRC assay, and this modified assay was considered to be useful as an antitumor sensitivity test.
IT 50924-49-7, Mizoribine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of subrenal capsule assay for sensitivity to anticancer drugs modified by combination with immunosuppressants)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 52 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:1007859 CAPLUS
DOCUMENT NUMBER: 140:59661
TITLE: Preparation of immunosuppressive poly-substituted pteridinediones (lumazines)
INVENTOR(S): Waer, Mark Jozef Albert; Herdewijn, Piet Andre Maurits Maria; Pfleiderer, Wolfgang Eugen
PATENT ASSIGNEE(S): 4 Aza Bioscience NV, Belg.
SOURCE: U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of U.S. Ser. No. 890,500, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030236255	A1	20031225	US 2003-444158	20030523
US 6946465	B2	20050920		
WO 2000045800	A2	20000810	WO 2000-EP938	20000202 <--
WO 2000045800	A3	20020110		

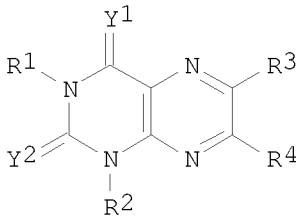
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1479682	A1	20041124	EP 2003-79183		20031224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
AU 2004240760	A1	20041202	AU 2004-240760		20040521
CA 2526651	A1	20041202	CA 2004-2526651		20040521
WO 2004104005	A2	20041202	WO 2004-EP5501		20040521
WO 2004104005	A3	20050127			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
EP 1636232	A2	20060322	EP 2004-734258		20040521
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
JP 2006528224	T	20061214	JP 2006-529892		20040521
US 20070043000	A1	20070222	US 2005-557541		20051121
PRIORITY APPLN. INFO.:			US 1999-118235P	P	19990202
			US 1999-118282P	P	19990202
			US 1999-118295P	P	19990202
			WO 2000-EP938	W	20000202
			US 2001-890500	B2	20011030
			US 2003-444158	A	20030523
			EP 2003-79183	A	20031224
			WO 2004-EP5501	W	20040521

OTHER SOURCE(S): MARPAT 140:59661

GI



I

AB The title compds. [I; R1 = H, alkyl, aryl, alkylaryl, etc.; R2 = H, alkyl, aryl, alkylaryl, etc.; R3, R4 = H, F, I, alkyl, etc.; Y1, Y2 = O, S; with provisos], useful as biol. active ingredients in preparing pharmaceutical compns. especially for the treatment or prevention of a CNS disorder, a cell proliferative disorder, a viral infection, an immune or auto-immune disorder or a transplant rejection, were prepared Thus, treating 1,3-dimethyllumazin-6-triphenylphosphonomethyl bromide (preparation given) with NaOMe in MeOH followed addition of pyridine-3-carboxaldehyde afforded 66% 1,3-dimethyl-6-[(E)-2-(pyrid-3-yl)vinyl]lumazine which showed IC50 of 30 μM in the mixed lymphocyte reaction (MLR) test which is considered as

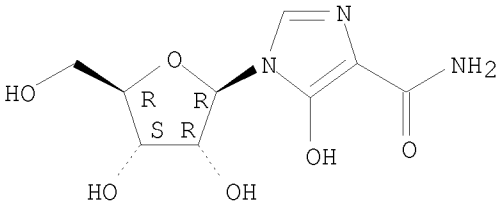
in vitro analog of the transplant rejection in vivo test. Combinations of the pteridine derivs. I with an immunosuppressant or immunomodulator drug, an antineoplastic drug or an antiviral agent, providing potential synergistic effects, are also disclosed.

IT 50924-49-7, Mizoribine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-administration; preparation of immunosuppressive pteridinediones for use in combination with other immunosuppressants)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 53 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1992:402498 CAPLUS

DOCUMENT NUMBER: 117:2498

ORIGINAL REFERENCE NO.: 117:531a,534a

TITLE: A QSAR model of teratogenesis

AUTHOR(S): Gombar, Vijay K.; Borgstedt, Harold H.; Enslein, Kurt; Hart, Jeffrey B.; Blake, Benjamin W.

CORPORATE SOURCE: Health Des., Inc., Rochester, NY, 14604, USA

SOURCE: Quantitative Structure-Activity Relationships (1991), 10(4), 306-32
CODEN: QSARDI; ISSN: 0931-8771

DOCUMENT TYPE: Journal

LANGUAGE: English

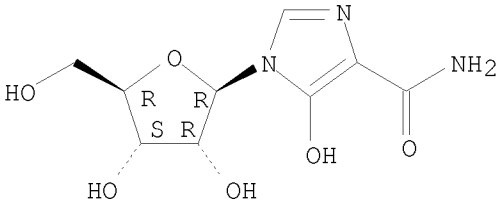
AB Four related QSAR models of teratogenesis in exptl. animals have been developed: one each for heteroarom., carboarom., alicyclic and acyclic compds. The nos. of compds. in these models range from 40 (for the alicyclic model) to 144 (for the carboarom. model). As determined by cross-validation using the leave-one-out, or jackknife, technique, the accuracy of the models in discriminating between teratogens and nonteratogens ranges from 92.4% to 96%. A single overall assessment of exptl. teratogenesis was chosen as the biol. endpoint; taking into account such factors as dosage, maternal toxicity, and affected organ systems remain to be subjects of further studies.

IT 50924-49-7, Bredinin
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(teratogenesis in laboratory animals from, QSAR model of)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 54 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:769087 CAPLUS
DOCUMENT NUMBER: 133:329580
TITLE: Use of rosmarinic acid and derivatives thereof as immunosuppressants or inhibitors of SH2-mediated processes
INVENTOR(S): Hur, Eun Mi; Choi, Young Bong; Park, Changwon; Lee, Jongsung; Park, Dongsu; Yun, Yungdae; Lee, Keun Hyeung; Oh, Jong-Eun; Ahn, Soon Choul; Lee, Hyun Sun; Ahn, Jong Sok; Jung, Soo Il
PATENT ASSIGNEE(S): Mogam Biotechnology Research Institute, S. Korea
SOURCE: U.S., 19 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6140363	A	20001031	US 1999-312405	19990514 <--
KR 2000072988	A	20001205	KR 1999-15989	19990504 <--
WO 9959606	A1	19991125	WO 1999-KR232	19990512 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1077715	A1	20010228	EP 1999-919691	19990512 <--
EP 1077715	B1	20060329		
R: CH, DE, ES, FR, GB, IT, LI, SE				
JP 2002526384	T	20020820	JP 2000-549270	19990512 <--
JP 3827948	B2	20060927		

PRIORITY APPLN. INFO.: KR 1998-17741 A 19980516
KR 1999-15989 A 19990504
WO 1999-KR232 W 19990512

AB The invention discloses the use of rosmarinic acid and/or derivs. thereof as immunosuppressive agents and/or inhibitors of SH2 domain function. Rosmarinic acid and derivs. thereof specifically inhibit the binding of ligand peptides to Lck SH2 domain, disturb the Lck-mediated signal transduction in T cells, also inhibit cytokine gene expression, and suppress immune responses in the transplanted tissue. These activities of rosmarinic acid and derivs. thereof support their applicability to treatment, prevention and/or diagnosis of graft rejection, graft-vs.-host disease, autoimmune diseases, inflammatory diseases, etc.

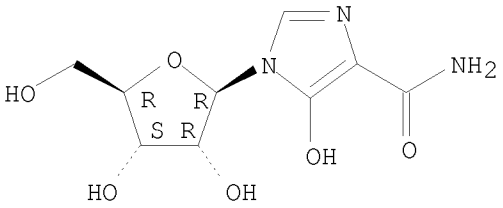
IT 50924-49-7, Mizoribine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 55 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:754988 CAPLUS

DOCUMENT NUMBER: 137:277799

TITLE: Anti-CD3 antibodies immunotoxins and immunosuppressant for treating autoimmune disease and transplant rejection

INVENTOR(S): Digan, Mary Ellen; Lake, Philip; Wright, Richard Michael

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 58 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020142000	A1	20021003	US 2000-480236	20000110 <--
AU 2000024370	A	20000801	AU 2000-24370	20000113 <--

PRIORITY APPLN. INFO.:

US 1999-232445	A	19990115
US 1999-236968	A	19990125
US 1999-414134	A	19991007
US 2000-480236	A	20000110
WO 2000-EP245	W	20000113

AB Recombinant immunotoxin polypeptides are described comprising a CD3-binding domain and a Pseudomonas exotoxin mutant, and in particular, comprising a single chain (s.c.) Fv as the CD3-binding moiety. A preferred species of the invention comprises scFv(UCHT-1)-PE38. Also disclosed are methods for the preparation of said immunotoxins; functionally equivalent immunotoxins which are intermediates in the preparation of the immunotoxins of the invention, as well as polynucleotide and oligonucleotide intermediates; methods for the prevention and/or treatment of transplant rejection and induction of tolerance, as well as treatment of autoimmune and other immune disorders, using the immunotoxins or pharmaceutically acceptable salts thereof; and pharmaceutical compns. comprising the immunotoxins or pharmaceutically acceptable salts thereof.

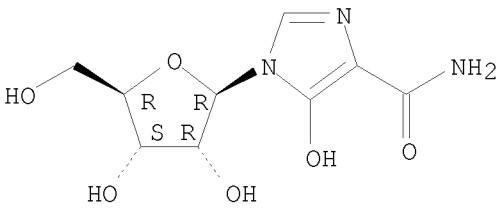
IT 50924-49-7, Mizoribine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(anti-CD3 antibodies immunotoxins and immunosuppressant for treating autoimmune disease and transplant rejection)

RN 50924-49-7 CAPLUS

CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 56 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:98696 CAPLUS

DOCUMENT NUMBER: 138:380608

TITLE: Evaluation and prevalidation of an immunotoxicity test based on human whole-blood cytokine release

AUTHOR(S): Langezaal, Ingrid; Hoffmann, Sebastian; Hartung, Thomas; Coecke, Sandra

CORPORATE SOURCE: European Centre for the Validation of Alternative Methods, European Commission Joint Research Centre, Institute for Health and Consumer Protection (ECVAM), Ispra, 21020, Italy

SOURCE: ATLA, Alternatives to Laboratory Animals (2002), 30(6), 581-595
CODEN: AALADQ; ISSN: 0261-1929

PUBLISHER: FRAME

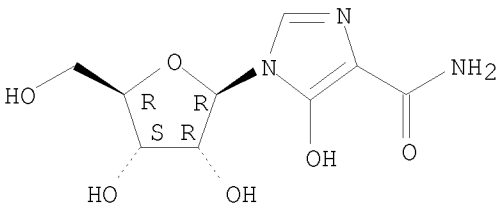
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Immunotoxicol. is a relatively new field in toxicol., and is one of emerging importance, because immunotoxicity appears to contribute to the development of cancer, autoimmune disorders, allergies, and other diseases. At present, there is a lack of human cell-based immunotoxicity assays for predicting the toxicity of xenobiotics toward the immune system in a simple, fast, economical, and reliable way. Existing immunotoxicity tests are mainly performed in animals, although species differences favor human-based testing. Whole-blood cytokine release models have attracted increasing interest, and are broadly used for pharmacol. in vitro and ex vivo studies, as well as for pyrogenicity testing. The authors have adapted those methods for immunotoxicity testing, to permit the potency testing of immunostimulants and immunosuppressants. Following stimulation with a lipopolysaccharide or staphylococcal enterotoxin B, monocytes and lymphocytes release interleukin 1β and interleukin 4, resp. Thirty-one pharmaceutical compds., with known effects on the immune system, were used to optimize and standardize the method, by analyzing their effects on cytokine release. The in vitro results were expressed as IC50 values for immunosuppression, and SC4 (4-fold increase) values for immunostimulation, and compared with therapeutic serum concns. of the compds. in patients, and in vivo LD50 values from animal studies. The in vitro results correlated well with the in vivo data, so the test appears to reflect immunomodulation. Results were reproducible (CV = 20 ± 5%), and the method could be transferred to another laboratory (r2 = 0.99). The authors therefore propose this method for further validation and for use in immunotoxicity testing strategies.

IT 50924-49-7, Mizoribine
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(evaluation and prevalidation of immunotoxicity test based on human whole-blood cytokine release)
RN 50924-49-7 CAPLUS
CN 1H-Imidazole-4-carboxamide, 5-hydroxy-1-β-D-ribofuranosyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 57 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:226300 CAPLUS
DOCUMENT NUMBER: 136:383898
TITLE: Identification of heat shock protein 60 as a molecular mediator of α3β1 integrin activation
AUTHOR(S): Barazi, Heba O.; Zhou, Longen; Templeton, Nancy Smyth; Krutzsch, Henry C.; Roberts, David D.
CORPORATE SOURCE: Laboratory of Pathology, National Cancer Institute, NIH, Bethesda, MD, 20892, USA
SOURCE: Cancer Research (2002), 62(5), 1541-1548
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The α3β1 integrin is involved in the adhesion of metastatic breast cancer cells to the lymph nodes and to osteoblasts in the bone. Regulation of the affinity or avidity of integrins for their ligands may result from conformational changes induced by changes in the microenvironment of the integrin. Two surface proteins, 55 and 32 kDa, coimmunopptd. with the α3β1 integrin from breast carcinoma cells. The 55-kDa protein preferentially associated with the active form of the α3β1 integrin. The protein was identified as HSP60 using two-dimensional electrophoresis and mass spectrometry and confirmed by reimmunopptn. of the integrin immune complex with an anti-HSP60 antibody. In cell spreading assays on a thrombospondin-1 substrate, addition of exogenous-recombinant HSP60 was sufficient to specifically activate α3β1 integrin but not to activate function of α2β1, αvβ3, α4β1, or α5β1 integrins. Furthermore, mizoribine, an HSP60-binding drug, blocked activation of the α3β1 integrin induced by insulin-like growth factor 1 (IGF1) or exogenous recombinant HSP60 and inhibited the association of HSP60 with the integrin. Addnl., inhibiting the surface expression of endogenous HSP60 by nonactin inhibited activation of the α3β1 integrin by IGF1. These data demonstrate that HSP60 binding is sufficient to activate α3β1 integrin function and suggest that association of endogenous HSP60 with α3β1 integrin is necessary for IGF1-induced activation.
REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 58 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:467405 CAPLUS
DOCUMENT NUMBER: 131:222847
TITLE: IMP dehydrogenase: structural aspects of inhibitor binding
AUTHOR(S): Goldstein, Barry M.; Colby, Thomas D.
CORPORATE SOURCE: Department of Biochemistry and Biophysics, University of Rochester Medical Center, Rochester, NY, 14642, USA
SOURCE: Current Medicinal Chemistry (1999), 6(7), 519-536
CODEN: CMCHE7; ISSN: 0929-8673
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB Inosine monophosphate dehydrogenase (IMPDH, E.C. 1.1.1.205) is recognized as an important target for both antileukemic and immunosuppressive therapy. A review with 118 refs. IMPDH catalyzes the NAD-dependent oxidation of inosine 5' monophosphate (IMP) to xanthosine 5' monophosphate. Several classes of IMPDH inhibitors are now in use or under development. These include agents that bind at either the substrate site (e.g. ribavirin and mizoribine) or at the NAD site (mycophenolic acid and thiazole-4-carboxamide adenine dinucleotide). All suffer from some degree of toxicity and/or susceptibility to metabolic inactivation. The finding that IMPDH exists as two isoforms, one of which (type II) is induced in tumor cells, has led to the search for potentially more effective isoform-specific agents. Recently, a number of crystal structures of IMPDH have become available. These include structures of the human type II, hamster, Tritrichomonas fetus, Streptococcus pyogenes and Borrelia burgdorferi enzymes. Each structure crystallizes as a tetramer of α/β barrels, with the active site located partly at the monomer-monomer interface. The substrate and cofactor bind in a continuous cleft on the C-terminal face of each barrel. The IMP base is well positioned to stack against the NAD nicotinamide ring to facilitate hydride transfer. The active site cleft is further bounded by a highly flexible flap and loop. These structures reveal enzyme-ligand interactions which suggest strategies for the design of improved inhibitors.
REFERENCE COUNT: 118 THERE ARE 118 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 17:18:33 ON 13 SEP 2008)

FILE 'REGISTRY' ENTERED AT 17:18:50 ON 13 SEP 2008
L1 2 S MIZORIBINE
L2 1 S INDANOCINE

FILE 'CAPLUS' ENTERED AT 17:19:45 ON 13 SEP 2008

FILE 'REGISTRY' ENTERED AT 17:19:59 ON 13 SEP 2008
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L3 SEL L1 1- CHEM : 10 TERMS
SET SMARTSELECT OFF

FILE 'CAPLUS' ENTERED AT 17:20:00 ON 13 SEP 2008
L4 564 S L3
L5 564 S L4 OR MIZORIBINE?

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                SET SMARTSELECT OFF

     FILE 'CAPLUS' ENTERED AT 17:20:15 ON 13 SEP 2008
L7            38 S L6
L8            38 S L7 OR INDANOCINE?

     FILE 'REGISTRY' ENTERED AT 17:21:03 ON 13 SEP 2008

     FILE 'CAPLUS' ENTERED AT 17:21:03 ON 13 SEP 2008

     FILE 'CAPLUS' ENTERED AT 17:21:17 ON 13 SEP 2008
L9           564 S L5 OR BREDININ OR HE 69 OR NSC 289637
L10           38 S L8 OR NSC 698666
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                E CANCER+ALL/CT
                E NEOPLASM+ALL/CT
                E LEUKEMIA+ALL/CT
L11           95 S L9 AND (CANCER OR TUMOR OR NEOPLASM OR NEOPLASTIC OR TUMOUR O
L12           14 S L10 AND (CANCER OR TUMOR OR NEOPLASM OR NEOPLASTIC OR TUMOUR
L13            2 S L11 AND L12
L14           58 S L11 AND PD<=2002
L15            3 S L12 AND PD<=2002
L16           58 FOCUS L14 1-

=> d ibib abs hitstr l15 1-3

L15  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2001:743261  CAPLUS
DOCUMENT NUMBER:          136:79386
TITLE:                    Biochemical genetic analysis of indanocine
                          resistance in human leukemia
AUTHOR(S):                Hua, Xuequn Helen; Genini, Davide; Gussio, Rick;
                          Tawatao, Rommel; Shih, Hsien; Kipps, Thomas J.;
                          Carson, Dennis A.; Leoni, Lorenzo M.
CORPORATE SOURCE:         Department of Medicine and The Sam and Rose Stein
                          Institute for Research on Aging, University of
                          California, San Diego, La Jolla, CA, 92093-0663, USA
SOURCE:                   Cancer Research (2001), 61(19), 7248-7254
                          CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER:                American Association for Cancer Research
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Indanocine is a potent tubulin-binding drug that is cytotoxic to
     multidrug-resistant cancer cell lines.  We demonstrated that
     indanocine specifically induces apoptosis in malignant B cells
     from patients with chronic lymphocytic leukemia.  To address the
     exact biochem. basis for indanocine toxicity, an
     indanocine-resistant clone was selected from mutagenized CEM human
     lymphoblastoid cells.  The resistant cells displayed a stable
     indanocine-resistant phenotype for at least 9 mo in drug-free
     culture.  The cloned cells are cross-resistant to colchicine and
     vinblastine, but not to paclitaxel, and do not have increased expression
     of the multidrug-resistant p170 glycoprotein.  In both parental cells and
     cell exts., indanocine treatment caused tubulin depolymn.  In
     contrast, the tubulin in the resistant clone did not depolymerize under
     identical conditions.  Both extract mixing and cell fusion expts. suggested
     that a stable structural change in microtubules, rather than a soluble
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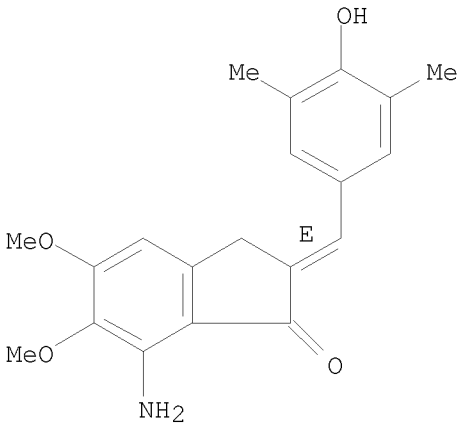
factor, was responsible for indanocine resistance. Sequence anal. of parental and resistant cells revealed a single point mutation in the M40 isotype of β-tubulin at nucleotide 1050 (G→T, Lys350→Asn) in the indanocine-resistant clone, in a region close to the putative colchicine binding site.

IT 265646-19-3, Indanocine
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biochem. genetic anal. of indanocine resistance in human leukemia in relation to a point mutation that prevents tubulin depolymn.)

RN 265646-19-3 CAPLUS
CN 1H-Inden-1-one, 7-amino-2,3-dihydro-2-[(4-hydroxy-3,5-dimethylphenyl)methylene]-5,6-dimethoxy-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:380438 CAPLUS
DOCUMENT NUMBER: 135:24657
TITLE: Selective cellular targeting: multifunctional delivery vehicles
INVENTOR(S): Glazier, Arnold
PATENT ASSIGNEE(S): Drug Innovation & Design, Inc., USA
SOURCE: PCT Int. Appl., 981 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001036003	A2	20010525	WO 2000-US31262	20001114 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2391534	A1	20010525	CA 2000-2391534	20001114 <--
AU 2001016075	A	20010530	AU 2001-16075	20001114 <--
EP 1255567	A1	20021113	EP 2000-978631	20001114 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 20030138432	A1	20030724	US 2000-738625	20001215

PRIORITY APPLN. INFO.:	US 1999-165485P	P 19991115
	US 2000-239478P	P 20001011
	US 2000-241937P	P 20001020
	WO 2000-US31262	W 20001114
	US 2000-712465	B1 20001115

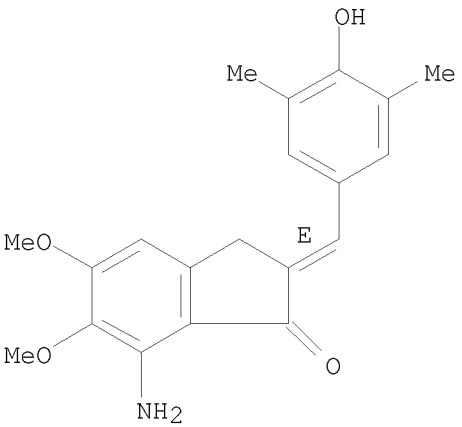
AB The present invention relates to the compns., methods, and applications of a novel approach to selective cellular targeting. The purpose of this invention is to enable the selective delivery and/or selective activation of effector mols. to target cells for diagnostic or therapeutic purposes. The present invention relates to multi-functional prodrugs or targeting vehicles wherein each functionality is capable of enhancing targeting selectivity, affinity, intracellular transport, activation or detoxification. The present invention also relates to ultralow dose, multiple target, multiple drug chemotherapy and targeted immunotherapy for cancer treatment.

IT 265646-19-3, Indanocine
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(multifunctional delivery vehicles for selective cellular targeting of drugs)

RN 265646-19-3 CAPLUS

CN 1H-Inden-1-one, 7-amino-2,3-dihydro-2-[(4-hydroxy-3,5-dimethylphenyl)methylene]-5,6-dimethoxy-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.

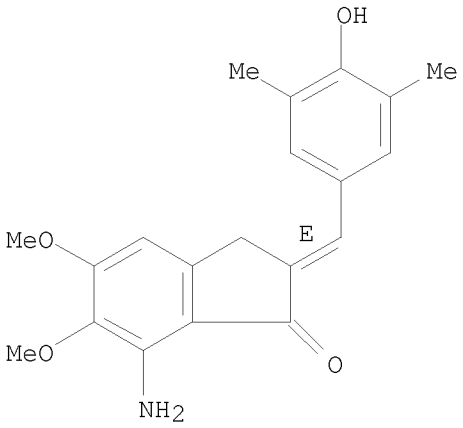


L15 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2000:110232 CAPLUS
DOCUMENT NUMBER:	133:37819
TITLE:	Indanocine, a microtubule-binding indanone and a selective inducer of apoptosis in multidrug-resistant cancer cells
AUTHOR(S):	Leoni, Lorenzo M.; Hamel, Ernest; Genini, Davide; Shih, Hsiencheng; Carrera, Carlos J.; Cottam, Howard B.; Carson, Dennis A.

CORPORATE SOURCE: Department of Medicine and The Sam and Rose Stein Institute for Research on Aging, University of California San Diego, La Jolla, CA, 92093, USA
SOURCE: Journal of the National Cancer Institute (2000), 92(3), 217-224
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Certain antimitotic drugs have antitumor activities that apparently result from interactions with nontubulin components involved in cell growth and/or apoptotic cell death. Indanocine is a synthetic indanone that has been identified by the National Cancer Institute's Developmental Therapeutics Program as having antiproliferative activity. In this study, we characterized the activity of this new antimitotic drug toward malignant cells. We tested antiproliferative activity with an MTT [i.e., 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide] assay, mitochondrial damage and cell cycle perturbations with flow cytometry, caspase-3 activation with fluorometry, alterations of the cytoskeletal components with immunofluorescence, and antimicrotubule activity with a tubulin polymerization assay. Indanocine is a cytostatic and cytotoxic indanone that blocks tubulin polymerization but, unlike other antimitotic agents, induces apoptotic cell death in stationary-phase multidrug-resistant cancer cells at concns. that do not impair the viability of normal nonproliferating cells. Of the seven multidrug-resistant cell lines tested, three (i.e., MCF-7/ADR, MES-SA/DX5, and HL-60/ADR) were more sensitive to growth inhibition by indanocine than were their corresponding parental cells. Confluent multidrug-resistant cells (MCF-7/ADR), but not drug-sensitive cancer cells (MCF-7) or normal peripheral blood lymphocytes, underwent apoptotic cell death 8-24 h after exposure to indanocine, as measured by sequential changes in mitochondrial membrane potential, caspase activity, and DNA fragmentation. Indanocine interacts with tubulin at the colchicine-binding site, potently inhibits tubulin polymerization in vitro, and disrupts the mitotic apparatus in dividing cells. The sensitivity of stationary multidrug-resistant cancer cells to indanocine suggests that indanocine and related indanones be considered as lead compds. for the development of chemotherapeutic strategies for drug-resistant malignancies.
IT 265646-19-3, Indanocine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(indanocine: microtubule-binding indanone and selective inducer of apoptosis in multidrug-resistant cancer cells)
RN 265646-19-3 CAPLUS
CN 1H-Inden-1-one, 7-amino-2,3-dihydro-2-[(4-hydroxy-3,5-dimethylphenyl)methylene]-5,6-dimethoxy-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT